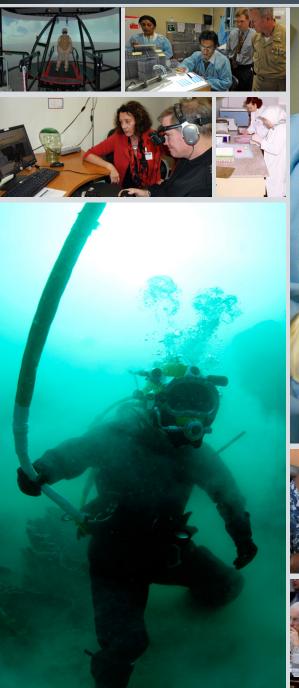
2ND ANNUAL NAVY MEDICINE RESEARCH AND DEVELOPMENT CONFERENCE

Conference Proceedings

"Connecting Wounded Warriors to Advanced Diagnostic and Therapeutic Options"

Uniformed Services University, Bethesda, Maryland, June 4-7, 2011













A Special Commemorative Edition of the Journal of Healthcare, Science and the Humanities

A Navy Medicine Publication

Published by the Navy Medicine Institute for the Medical Humanities and Research Leadership, USN Bureau of Medicine and Surgery in partnership with the Smithsonian Institution.

The Journal of Healthcare, Science and the Humanities

General Information

In cooperation with the Smithsonian Institution, *The Journal of Healthcare, Science and the Humanities* is published by the Navy Medicine Institute for the Medical Humanities and Research Leadership, USN Bureau of Medicine and Surgery, Washington, DC, USA. As an agency of Navy Medicine, the Institute supports the mission of the Navy Surgeon General and Navy Medicine itself for force health protection and readiness. The Institute is dedicated to the academic enrichment and professional development of Navy Medicine leaders and their collaborators in other federal agencies, in institutions of higher learning, and in private agencies around the world. Representing all of the arts and sciences related to healthcare, the Institute serves as an international academy serving Navy Medicine by enriching its mission of scholarship and innovation in systems healthcare and professional excellence on behalf of the public trust. ISSN (print): 2159-8800. ISSN (online): 2159-8819.

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Manuscripts are to be submitted to the Editor. Submission of a manuscript is considered to be a representation that it is not copyrighted, previously published, or concurrently under consideration for publishing in print or electronic form. Contact the *JHSH* Editor for specific information for authors, templates, and new material. The preferred communication route is through email at Journal@med.navy.mil. To obtain copies, individuals may email the Executive Leadership at Journal@med.navy.mil or call (202) 762-3817. *Journal* issues are available for download from the Navy Medicine Veterans and Alumni Association.

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The Editor-in-Chief and the Journal Executives express their gratitude to the following who generously volunteered personal time and effort to edited the materials herein after initial Conference Leader submission and review:

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The materials found in this commemorative edition were initiated and reviewed by the Conference Leaders themselves. They then submitted the materials to the Journal.

With gratitude are noted those who generously provided for all initial processes including Dr. Wayman Cheatham, Dr. Kenneth Green, and other members of the Navy Medicine Research and Development Center.

The Journal of Healthcare, Science and the Humanities



Published in cooperation with the Smithsonian Institution.



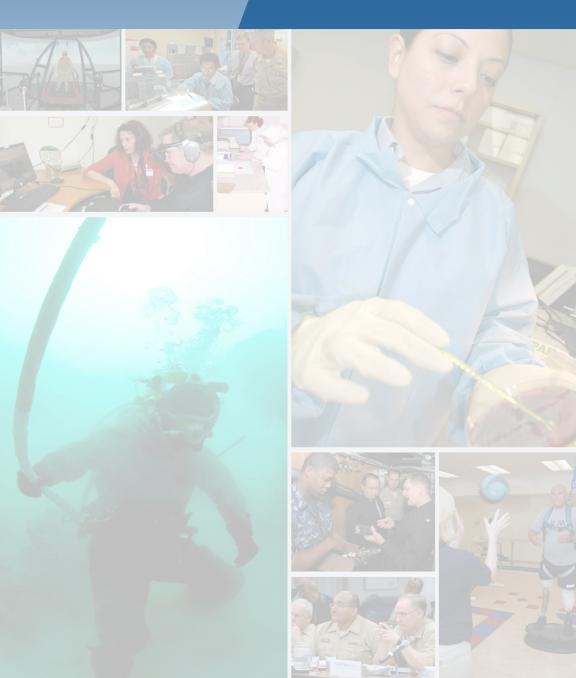
Prepared by Graphic Arts and Publishing Services at The Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc.

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FROM THE EDITOR'S DESK





From the Editor's Desk

Dr. Edward F. Gabriele

Editor, Journal of Healthcare, Science and the Humanities Deputy Vice Chancellor, Navy Medicine Institute for the Medical Humanities & Research Leadership USN Bureau of Medicine and Surgery Washington, DC 20352 Tel: (202) 762-3600

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Without question, all of us realize that research and development are central to our continual advancement as members of the world community. Despite all of the many regulatory or required definitions that nations and communities may author and espouse, in every academic and professional discipline research can rightly be defined as "genius becoming innovation." The way forward for human cultural and personal advancement begins with that inner spark of genius that moves the academic, the scholar, and the researcher to explore and discover, to experiment and test, to entertain the unforeseen and wander among the elements of the unpredictable. The sparks of such genius are absolutely central to stoking the luster and warmth of medicine and healthcare in all of their arts and sciences and technologies.

In 2012, Navy Medicine will remember the 70th anniversary of the founding of what is today its central biomedical research laboratory. In a certain respect, this moment of historical celebration comprises a type of living portal through which the Navy Medicine Community will step into the central pathway of every form of research and development that inspires our healthcare leaders to stand ever more closely to those who come to us for healing. However such living-recall is not limited to actual celebration years. Our remembrance of the importance of who we are and what we do is at the roots of the professions of care we have embraced. Hence, in each year Navy Medicine researchers and scientists gather together to celebrate what has been accomplished, to share what yet must be done, and to dream out loud for what might be.

This Special Commemorative Edition of the Journal of Healthcare, Science and the Humanities captures materials presented at the June 2011 Research and Development Conference sponsored by the Navy Medicine Research and Development Center. In this edition, you will find the invitation from the Center Director, the Conference Agenda, the Opening Keynote of the Navy Surgeon General, Keynote Summary Materials representing lecture information from several of the keynote speeches, presentation abstracts, and poster abstracts. These represent information already shared or presented. They also capture well much that is transpiring today to secure the health and wellness of those in need. More so, we hope that the impact of these next pages will elevate your own energies—to appreciate "what is" in the hope of "what might be." And in all of this, perhaps each of us can be led to wonder where in our own lives we too might become more "ingenious and innovative" to care for those we meet in every walk of our lives.

Computational Analysis and Optimization Wound Closure

Shelby G. Topp LT MC USN, Curtis Gaball LCDR MC

Department of Otolaryngology – Head and Neck Surgery, Naval N

INTRODUCTION

The rhombic local skin flap is a commonly used method for closure of facial cutaneous defects. Initially described by Limberg in 1928, it has maintained its popularity in large part due to its predictable results and versatility. A multitude of variations of rhombic flap geometry have been published as distinct entities; all are based on the principle of local skin transposition to fill a defect from an adjacent donor site. One important attribute of these and all local flap wound closures is the distribution of wound closure forces across the incision lines and surrounding tissues, which impacts the favorability of wound healing and scar formation. Excess wound tension can lead to unfavorable scarring and wound breakdown. Closure forces are determined by skin and soft tissue elastic properties, which have been modeled using the finite element method, as first applied to wound closures by Larrabee. The current study seeks to develop a computational model using the finite element method for the analysis of wound closure forces in an effort to optimize an idealized rhombic flap design.

METHODS

A computational model was designed to analyze rhombic flap closures to include variables of transposition angle, flap width, distal angle, and degree of tissue undermining. Outcome measures of tissue stress, tissue strain, and wound distortion were evaluated. Design variables were manipulated to include analysis of the rhombic variations described by Dufourmental and Webster The basic flap geometry with modeled variables is shown in Figure 1 below.



Figure 1: Rhombic flap model geometry

First Principal strain is defined as strain in the plane of the skin surface.

Z-direction strain is defined as strain in the direction perpendicular to the plane of the skin surface, and functions as ar indicator of standing cutaneous deformity with wound closure.

A two-dimensional nonlinear finite element model was used to simulate defect closure and suturing, with planar visualization of wound area directional stress and strain. This was performed as a two-dimensional planar geometry in the ANSYS 11.0 software package. Modeling characteristics for skin were commensurate with previously published finite element studies based on experimental skin elasticity measurements 4 . Skin material properties were modeled as nonlinear and hyperelastic, fit to a 2nd order Yeoh model defined with $C_{10}=0.017207,\,C_{20}=0.19287,\,$ and $d_1=d_2=0$.

RESILITS

Classic Limberg flap

The model was first solved for the classic Limberg flap (α = 0, β = 60) with a defect having interior angles of 60° and 120°. The figures below illustrate skin displacement, strain, and stress for this closure. Areas of maximal tissue displacement and incision line tension are depicted and are consistent with those predicted from clinical experience.



Figure 2: clockwise from top left a)Limberg flap skin displacement, b) tissue principal strain, and c) tissue principal stress

From the baseline Limberg solution, alterations in defect height, flap transposition angle, and flap width were specifically analyzed

Effect of Defect Height

Varying defect height while holding width constant demonstrates two major findings:

 Peak principal strain increases as defect height increases from a initial square defect

2.Z-direction strain is minimized with the classic Limberg defect (e.g. interior angles of 60° and 120°), indicating a minimized standing cutaneous deformity (i.e. dog-ear)



Figure



figure 4: clockwise from top left - a) principal strain with square lefect, b) Limberg defect of 60° and 120°, c) 1.5x greater vertical limension than Limberg

on of the Rhombic Flap

USN, and Scott Lovald PhD



RESULTS

Effect of Transposition Angle

The Dufourmental rhombic modification, with altered flap transposition angle (corresponding to the a angle in the model), was initially designed to broaden rhombic applications to defects not conforming to the 60°-120° Limberg configuration. The model was solved for the Limberg defect and a square defect. The results, as depicted below, show that increasing transposition angle can decrease principal strain for the Limberg defect, but increases strain for a square defect.



Figure 5: Effect on peak strain seen with alteration of transposition angle for a) Limberg defect and b) square defect

Additionally, alteration of flap transposition angle impacts the directional closure force vector, as shown in Figure 6.



Figure 6: Depiction of altered primary closure force vector with alteration of transposition angle, with increase from a) α = 0 to b) α = 50

Effect of Flap Width

The Webster modification of the rhombic flap alters flap width and has a defined distal angle of 30°, and also incorporates a W-plasty into the defect closure to minimize standing cutaneous deformity. This closure essentially provides donor tissue volume smaller than that of the defect, and relies on adjacent wound margin skin advancement, termed secondary tissue movement. In the model, B angle modification demonstrates properties of the Webster flap. Figure 7 below shows that the Webster 30° B angle confers lower principal strain for the Limberg-configuration defect, while it shows an increased principal strain for a square defect.



Figure 7: Effect of changing flap width (e.g. Webster angle) for a)

CONCLUSION

The model visually depicts quantitative properties of rhombic flap closures, and as such can be of value to the surgeon designing local flap closures. Specific principles shown include:

- Reducing the Webster angle distributes tissue strain to the side of the defect opposite the donor site, which can reduce peak principal strain but may exert force on a nonmobile structure (e.g. nose or eyelid) in an unfavorable way.
- -A change in the Dufourmental angle has a strong effect on orienting the closure strain field, and may be usefully employed to align a closure into a favorable relationship to lines of maximal extensibility and relaxed skin tension lines, which are intrinsic properties specific to a defect location.
- Strain images from the model provide surgeons a more complete understanding of tissue strains surrounding a defect closure when compared to traditional teaching, which emphasizes the single force vector at the point of maximal tension.
- An idealized rhombic flap closure, assuming equal skin elastic properties in all directions, would be constructed with a Webster angle of 30° and Dufourmental angle of 0° (as in the classic Limberg design), as shown in Figure 8.



Figure 8: Idealized rhombic flap closure, with Webster (B) angle : 30° and Dufourmental angle (α) = 0°

REFERENCES

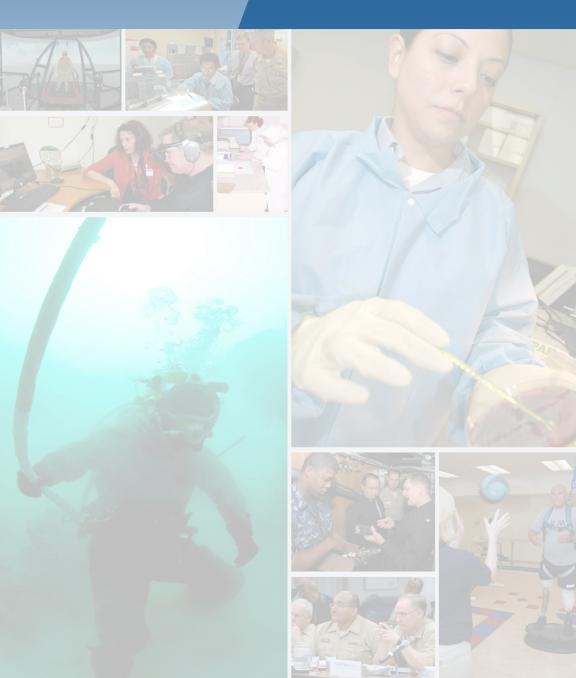
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ACKNOWLEDGMENTS

The authors would like to thank Dr. Tariq Khraishi for his assistance with software use and coding for creation of the model.



CONFERENCE INTRODUCTION





Navy Medicine Research and Development Conference Connecting Wounded Warriors to Advanced Diagnostic and Therapeutic Options

Conference Introduction

Wayman Wendell Cheatham, MD, FACE

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Email: Wayman.Cheatham@med.navy.mil

The opinions in these remarks are those of the author and do not represent the views of Navy Medicine, the Department of the Navy, the Department of Defense, or the United States Government.

This conference, held on June 4–7, 2011 at the Uniformed Services University of the Health Sciences in Bethesda, Maryland, was intended to showcase those medical research topics that have been identified by the Secretary of Defense, the Navy Surgeon General, and other Navy research strategists as priorities upon which to focus medical research efforts. The meeting agenda focused on those areas where significant research gaps exist, which, if closed, will significantly benefit both the war fighter and other Navy enterprise wide beneficiaries.

This venue was the only United States Navy Medicine research conference of the year bringing together Navy researchers and civilian counterparts to showcase the efforts being made on research priorities and gaps as defined by the Navy Surgeon General and the Secretary of Defense.

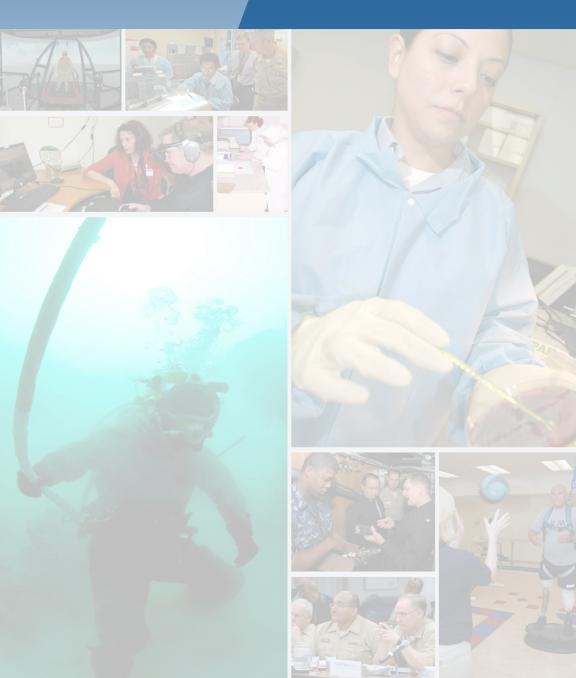
The topics discussed have direct impact on the direction of current and future research plans that will directly impact the ability to deliver improved care to our warfighters, our wounded warriors, and to the Navy enterprise as a whole; and will have shared impact on sister services' care of their beneficiaries.

The presence of several notable internationally recognized researchers from the civilian academic and Navy medical research communities was unique to this Navy forum. The information they had to share was significant in providing "game changing" insight into how we might care for patients going forward.

The results of information presented at this conference will have significant and positive impact on all beneficiaries throughout the Navy enterprise, the United States Department of Defense, and the Global Population, as a whole.



CONFERENCE AGENDA





2nd Annual Navy Medicine Research Conference **Connecting Wounded Warriors to Advanced Diagnostic and Therapeutic Options**

4-7 June 2011 **Uniformed Services University of the Health Sciences**

Saturday 4 June

1100-1700	Conference Registration	USUHS Bldg. B Lobby	
1200-1500	Nurse Researchers Pre-meeting	NNMC-America Building (2nd floor) Room 2301	
	CAPT Patricia A.W. Kelley (NC) USN		
	Deputy Director Nursing and Allied Health Research,		
	Navy Medicine Research & Development Center		
	Navy Medicine Institute, Bureau of Medicine & Surgery		
1800-2100	Welcoming Dinner	USUHS Bldg. B Dining Facility	

A Comprehensive Overview of the Navy Medicine Research Enterprise

Wayman Wendall Cheatham, MD, FACE Special Assistant to the Navy Surgeon General for Medical Research Director, Navy Medicine Research & Development Center Navy Medicine Institute, Bureau of Medicine & Surgery

Sunday 5 June (USUHS Building D, Lecture Hall D, 1st Floor)

0930	Coffee
1000	Meeting Welcome & Logistics CDR Ken Green Associate Director for Research Operations Integration Medical Research & Development Center Navy Medicine Institute, Bureau of Medicine & Surgery
1005	Opening Ceremony Color Guard–USUHS Color Guard National Anthem Invocation

1020 Welcoming Remarks/Introduction of Keynote Speakers

Wayman Wendall Cheatham, MD, FACE Special Assistant to the Navy Surgeon General for Medical Research Director, Navy Medicine Research & Development Center Navy Medicine Institute, Bureau of Medicine & Surgery

1030 Keynote Welcoming Address

Vice Admiral Adam M. Robinson, Jr. The Surgeon General of the United States Navy Chief, Bureau of Medicine & Surgery

1100 ONR Human Systems Science & Technology: RDT&E Partnerships

Dr. Terry Allard Department Head, Warfighter Performance Science and Technology Office of Naval Research, Arlington, VA

1130 From the Neuroscience of Neural Injury to a Neuroethics of Care: Implications for Navy Research and Medicine

Dr. James Giordano Director, Center for Neurotechnology Studies, Vice-President, Academic Programs Potomac Institute for Policy Studies, Arlington, VA

1200 Lunch USUHS Cafeteria

Traumatic Brain Injury/Neurotrauma Track

1300 Keynote: TBI and Neuroinflammation: A Rationale for Treatment

Dr. Joseph Maroon Professor and Vice Chairman Department of Neurosurgery Heindl Scholar in Neuroscience University of Pittsburgh Medical Center Team Neurosurgeon Pittsburgh Steelers

1330 Role of Transcranial Doppler Ultrasound in Evaluation of Patients after Traumatic Brain Injury

Alex Razumovsky, PhD, FAHA, Director of Sentient NeuroCare Services, Baltimore, MD

COL Rocco A. Armonda (MC) USA Director of Cerebrovascular Surgery and Interventional Neuroradiology, National Naval Medical Center, Bethesda, MD

1345 A Novel Management Strategy for the Treatment of Penetrating Brain Injury Pseudoaneurysms

Teodoro Tigno, M.D.

Senior Research Scientist, HJF

Neurosurgery Service, Dept. of Surgery

Walter Reed Army Medical Center/National Naval Medical Center

1400 Repeated Exposure to Low Level Blast Overpressure Produces Impairment in Acquisition of Spatial Information

Stephen Ahlers, Naval Medical Research Center, Silver Spring, MD

1415 An fMRI Study of TBI Associated with Blast Injury

Joseph McArdle, PhD,

Naval Medical Research Center, Silver Spring, MD

1430 BREAK Poster Session (A Presenters)

A Digital Cranium Model for Prediction of Functional Deficits in Traumatic 1500 **Brain Injury**

Albert Bailey, PhD TASC, Inc.

1515 Identifying Biomarkers that Distinguish Post Traumatic Stress Disorder and Traumatic Brain Injury Using Advanced Magnetic Resonance Spectroscopy

Alexander P. Lin, PhD.,

Instructor, Harvard Medical School

Clinical Spectroscopist, Brigham and Women's Hospital, Boston, MA

1530 A Processing Pipeline for in vivo Brain Magnetic Resonance Spectroscopy for Diagnosing and Treating Neurotrauma

Nirmal Keshava, PhD

Group Leader,

Fusion, Exploitation, and Inference Technologies Group

Charles S. Draper Laboratory, Cambridge, MA

1545 Session Q&A

PTSD & Behavioral Health Track

1600 The Relationship between Mental Health Disorders and Reenlistment Status among Enlisted U.S. Marine Corps Personnel

Emily Schmied, MPH, Naval Health Research Center, San Diego, CA

Patterns of Post-Traumatic Stress Symptoms, Substance Abuse and Depression among Deploying U.S. Marines

Valerie Stander, PhD, Naval Health Research Center, San Diego, CA

1630 Preparing for the Stress of Combat: The DOCS Graphic Novel and Video Animation

Katie Shobe, PhD, Heidi Kraft, PhD, and Jerry Larson, PhD, Naval Health Research Center, San Diego, CA

1645 Post Traumatic Stress Disorder a Persistent Diagnostic Challenge

Hamid Tavakoli, M.D., Department of Psychiatry, Naval Medical Center, Portsmouth, VA

1700 Altered Parietal Cortex Activations in Response to Emotional Pictures in Subjects with PTSD and TBI

Julie Onton, PhD, Neuroscientist, Naval Health Research Center. San Diego, CA

1715 Session Q&A

1730 Adjourn for the day

Monday 6 June (USUHS Building B, Sanford Auditorium)

0730 **Coffee**

Wound / Injury Management throughout the Continuum of Care

0800 Keynote: Immune Modulation for Hand Transplantation—Changing the Risk-Benefit Balance

W. P. Andrew Lee, M.D. The Milton T. Edgerton, MD, Professor and Chairman, Department of Plastic & Reconstructive Surgery Johns Hopkins University School of Medicine

0900 Nanotechnologies and Hemostatic Agents

Rutledge Ellis-Behnke, PhD
Department of Brain & Cognitive Sciences,
Massachusetts Institute of Technology, Cambridge, MA

Bringing Novel Clinical Advances from the Bench to the Bedside: Translational 0930 Medicine at the Naval Health Research Centre CDR Dennis Faix (MC) Naval Health Research Center, San Diego, CA 0945 Evaluation of Intestinal Viability Using 3-CCD (Charge Coupled Device) in Children Undergoing Appendectomy Maridelle Millendez, MD, Department of Surgery, National Naval Medical Center, Bethesda, MD 1000 Session Q&A 1015 BREAK Poster Session (B Presenters) 1045 Analysis of Navy-Marine Corps En Route Care (ERC) in OIF and OEF CDR Amy McBride (NC) Department Head Critical Care, Naval Medical Center Portsmouth, VA 1100 Pyschometric Evaluation of a Triage Decision Making Inventory CDR Anita Smith (NC) University of South Alabama, Mobile, AL 1115 Interactive Rich-Medi, Self-Documenting System on Handheld Devices for Medical Procedure and Decision Support M. Sriram Iyengar, PhD Assistant Professor of Biomedical Informatics The University of Texas Health Science Centre at Houston

1130 A Stranger in a Strange Land: Interventional Radiology in Kandahar, Afghanistan

> CDR John York, (MC) (FS) Section Chief, Interventional Radiology, Naval Medical Center Portsmouth, VA

1145 Session Q&A

Lunch USUHS Cafeteria 1200

1300 Determining the Effects of Multiple Mechanisms of Injury Due to Explosions on Casualty Outcome in the Shipboard Setting

Howard Champion, MD President/CEO SimQuest, LL Naval Health Research Center, San Diego, CA

New Tools for Characterizing Shipboard Injury: Military Combat Injury Scale (MCIS) and Military Functional Incapacity Scale (MFIS)

Howard Champion, MD President/CEO SimQuest, LL Naval Health Research Center, San Diego, CA

1330 Joint Combat Casualty Research Team (JC2RT)—Lessons Learned in facilitating In Theater Research Initiatives

Lisa Osborne, PhD, CRNA Research Director, Uniformed Services University Nurse Anesthesia Program Deputy Director, Joint Combat Casualty Research Team, Team 9

1345 Restoration of Internal Models of Grasp in Users of Myoelectric Prosthetic Hands

Alexander Dromerick, MD, Peter Lum, PhD, National Rehabilitation Hospital, Washington, DC

1400 BREAK Poster Session (C Presenters)

1430 Imaging, Modeling, and Rapid Prototype techniques in Craniofacial Reconstruction

Gerald T. Grant, DMD, MS Director Craniofacial Research Integrated Service Chief, 3D Medical Applications Naval Postgraduate Dental School, Bethesda, MD

1445 Accuracy of Rapid Prototype Models for Head and Neck Reconstruction

CAPT Robert Taft (DC) Dean, Naval Postgraduate Dental School, Bethesda, MD

1500 Comparison of Mechanical Work during Walking between Military Patients with Traditional and Ertl Transtibial Amputations

Marilynn Wyatt, MA, PT Director of Biomechanics Laboratory Naval Medical Center San Diego, CA

1515 A Promising Platform for Malaria Vaccines: Results from a Clinical Trial of a DNA Prime-Adenovector Boost Regimen to Prevent Plasmodium falciparum Malaria

CDR Ilin Chuang, (MC), US Military Malaria Vaccine Program, Naval Medical Research Center, Silver Spring, MD

1530 Session Q&A

1545 BREAK

26th Annual Navy Wide Research Competition Presentations

1600 National Capital Region Annual Research Competition Trainee Winner:

Lypholized Platelet Transfusion Does Not Constitute an Immunologic "Second Hit" in a Non-Human Primate Hemorrhagic Shock Model

LT Alan Strawn (MC) Department of Surgery, National Naval Medical Center, Bethesda, MD

1615 Navy Medicine West Annual Research Competition Winner:

Tourniquets Exposed to Afghanistan Combat Environment Have Decreased Efficacy and Breakage Compared with Unexposed Tourniquets

LCDR Richard Childers, MC, USN, Emergency Medicine Department, Naval Hospital Camp Pendleton

1630 Navy Medicine East Annual Research Competition Trainee Winner:

A Comparison of the Prophylactic Combination of Palonosetron and Dexamethasone versus Ondansetron and Dexamethasone on the Incidence and Severity of Post-Discharge Nausea and Vomiting in a Group of High Risk Patients

LT Kevin Michel (NC), CRNA, Naval Medical Center Portsmouth, VA

1645 National Capital Area Annual Research Competition Staff Winner:

Study of the Seroconversion of Helicobacter Pylori Infection among U.S. Military Deployed in Operation Iraqi Freedom

LCDR Ruben Acosta (MC) National Naval Medical Center, Bethesda, MD

1700 Navy Medicine West Annual Research Competition Staff Winner:

Lung Inflammation and Altered Pulmonary Functions in Animals Following **Lung Blast Exposure**

LT James Prahl (MC) Naval Medical Center San Diego, CA

1715 Navy Medicine East Annual Research Competition Staff Winner:

> The Effect of Intraoperative Intravenous Lidocaine Infusion on the Reduction of Postoperative Pain and Return of Bowel Function in Patients undergoing Minor Laparoscopic Gynecological Procedures

> > CDR Greg Nezat CRNA, PhD (NC), Department Head Nursing Research Naval Medical Center Portsmouth, VA

1730 Session Q&A

1745 Adjourn for the day

Tuesday 7 June (USUHS Building B, Sanford Auditorium)

Coffee 0730

0800 Keynote: Use of Adipose Derived Stem Cells for Wounded Warrior Care

> J. Peter Rubin, M.D. Associate Professor of Plastic & Reconstructive Surgery University of Pittsburgh Medical Center

0900 Predicting Individual Fatigue Resistance: Implications for Casualty Prevention through Optimized Crew Scheduling

> Jeffrey Phillips, PhD, Naval Aerospace Medical Research Laboratory, Pensacola, FL

0915 Domestic Violence Screening of Obstetric Triage Patients in a Military Population

> CAPT Paul Rockswold (MC) Head, Health Analysis Department Navy and Marine Corps Public Health Center, Portsmouth, VA

0930 Does Testing Positive for Gonorrhea or Chlamydia in the First Trimester of Pregnancy Affect Fetal Outcomes?

> LT Diana Macian (MC) Naval Medical Center Portsmouth, VA

0945 BREAK (last poster availability)

1000 The Potential Effect of Jet Fuel Exposure on Noise Induced Hearing Loss

LT Pedro Ortiz, PhD (MSC) Naval Medical Research Unit Dayton Wright-Patterson Air Force Base, Ohio

1015 Impulse Noise Hearing Loss Prevention Using N-acetylcysteine

LT Caroline Messmer, (MC) Department of Otolaryngology PGY-4 Naval Medical Center San Diego, CA

1030 Effects if Tympanomeatal Blunting on Sound Transfer Function

David Mullin, MD Department of Otolaryngology Naval Medical Center San Diego, CA

1045 Effects of Hyperbaric Hyperoxic Stress on Expired Nitric Oxide and Expired Carbon Monoxide in Divers

David Fothergill, PhD Naval Submarine Medical Research Laboratory, Groton, CT

1100 Submariner Health: Experimental Evaluation of Exposure Limits for Key **Inhaled Compounds**

Michael Gargas, PhD Director, Environmental Health Effects Research Directorate Naval Medical Research Unit Dayton Wright-Patterson Air Force Base, Ohio

1115 Using Vigabatrin for Reducing the Incidence of CNS Oxygen Toxicity Associated with Oxygen Pre-Breathe at 132 FSW

Aaron Hall, PhD, Associate Investigator, Undersea Medicine Department Naval Medical Research Center, San Diego, CA

1130 **Overall Winner Announcement** Navy Research Competition

1145 Closing Remarks

Wayman Wendall Cheatham, MD, FACE Special Assistant to the Navy Surgeon General for Medical Research Director, Navy Medicine Research & Development Center Navy Medicine Institute, Bureau of Medicine & Surgery

1150 Meeting Adjourns

Poster Sessions

Presenters will be available near their posters at the assigned times for their group, to answer questions about their research/project. (Posters will be displayed in the covered breezeway between USUHS Building B and Building D)

A Group

1. Assessment of Environmental Tobacco Smoke Exposure

Linda Hughes, Naval Submarine Medical Research Laboratory, Groton, CT

2. Risk Analysis Program for U.S. Navy Submarine Escape Training

Linda Hughes, Naval Submarine Medical Research Laboratory, Groton, CT

3. Improved Submariner Eyewear for Routine Wear and Emergency Equipment Use Underway

Alison America, MA, Naval Submarine Medical Research Laboratory, Groton, CT

4. The Role of Military Occupation on New-Onset Post-Traumatic Stress Disorder and Depression Diagnosis among Personnel Deployed to Iraq

Andrew MacGregor, PhD, Naval Health Research Center, San Diego, CA

5. Prevalence and Auditory Effects of Blast Related Ear Injury in Operation Iraqi Freedom

Andrew MacGregor, PhD, Naval Health Research Center, San Diego, CA

6. Trends in Post-Concussive Symptoms Reporting Following Mild Traumatic Brain Injury in Operation Iraqi Freedom

Andrew MacGregor, PhD, Naval Health Research Center, San Diego, CA

- Non-Combat Motor Vehicle Accidents during Operation Iraqi Freedom
 Andrew MacGregor, PhD, Naval Health Research Center, San Diego, CA
- 8. The New Zealand Breacher Study: Blood Brain Biomarkers, Neuro-Cognitive Performance and Self-Reported Symptoms

Stephanie Eonta, Naval Medical Research Center, Silver Springs, MD

9. Perfluorocarbon (PFC) Administration Decreases Mortality in a Rat Model of Decompression Sickness

LT Kevin Marrs (MSC) PhD, Undersea Medicine Department Naval Medical Research Center, San Diego, CA

10. Perflourocarbon Treatment of DCS

Charles Auker, MD, PhD, Principle Investigator, Undersea Medicine Department Naval Medical Research Center, San Diego, CA

11. Acute Mountain Sickness at Moderate Elevation

Erik Viirre M.D. Ph.D. Senior Scientist, Warfighter Performance Naval Health Research Center, San Diego, CA

B Group

1. Extra Amniotic Balloon for Pre-Induction Cervical Ripening: A Randomized Comparison of Weighted Traction vs. Non-Weighted

> LCDR Monica Lutgendorf (MC), Department of Obstetrics and Gynecology Naval Medical Center Portsmouth, VA

2. Profile of Pediatric Admissions to the USNS Comfort Following the 2010 Haiti Earthquake, Lessons for Future Hospital Ship Based Disaster Relief Missions

Mathew McLean, M.D., Naval Medical Center Portsmouth, VA

3. **Humanized Mouse Models for Human Diseases**

> Sofia Casares, PhD, Senior Immunologist, US Military Malaria Vaccine Program Naval Medical Research Center, Silver Springs, MD

4. Identification of Next-Generation In-Cockpit Oxygen Sensors to Reduce **Hypoxia-Related Casualties**

R. E. Dory, Naval Aerospace Medical Research Laboratory, Pensacola, FL

- 5. Aviation Casualty Prevention through Applied Spatial Disorientation Research R. E. Dory, Naval Aerospace Medical Research Laboratory, Pensacola, FL
- 6. Benchmarking to the International Pressure Ulcer Prevalence Survey LCDR Sharon House (NC), Naval Medical Center Portsmouth, VA
- 7. Burn Pit Smoke Exposure and Health Risks in the Millenium Cohort Study Kelly Jones, MPH, Naval Health Research Center, San Diego, CA
- 8. The DoD ACAM2000 Smallpox Vaccine Myopericarditis Registry A. S. Conlin, Naval Health Research Center, San Diego, CA

9. The Early Post-Hemorrhage Coagulation Profile Is Characterized by Qualitative Platelet Dysfunction

Alan Strawn, M.D., Department of Surgery, National Naval Medical Center, Bethesda, MD

10. Computational Analysis and Optimization of the Rhombic Flap Woud Closure

LT Shelby Topp (MC), Department of Otolaryngology, Naval Medical Center San Diego, CA

11. Visual Performance and Hypoxia: A Dual Threat to Aviator Safety

LCDR Hong Gao, OD, PhD, Aerospace Optometrist (MSC) Naval Aerospace Medical Research Laboratory, Pensacola, FL

12. Retinoid Signaling by a Selective Retinoid Acid Receptor Agonist Hinders Angiogenesis, Formation of Granulation Tissue and Wound Closure in Cutaneous Models of Wound Healing

Steven Grijalva, MD, Regenerative Medicine Department, Naval Medical Research Center, Silver Spring, MD

C Group

1. Comparison of Cone Beam CT and Conventional CT in Accuracy of Rapid Prototype Models: Image Registration

Shayne Kondor MSAE, Chief Engineer, Craniofacial Research Naval Postgraduate Dental School

2. A Chaotic Analysis Method for Examining Speech

Elena Polejaeva, Naval Medical Research Center, San Diego, CA

3. Monitoring Cortical Hypoxia Using Near-Infrared Spectroscopy: Research and Application for Aviation Mishap Prevention

Jeffrey Phillips, PhD, Naval Aerospace Medical Research Laboratory, Pensacola, FL

4. To Investigate the Influence of Acute Vestibular Impairment Following Mild
Traumatic Brain Injury on Subsequent Ability to Successfully Complete a
Vestibular Physical Therapy Program and Remain on Active Duty One Year Later

Kim Gottshall, PhD, Naval Medical Center San Diego, CA

Accessing Intra-individual Variability after TBI using Grip Force 5. **Dynamometry**

> Alexander Dromerick, MD, National Rehabilitation Hospital, Washington, DC

6. **Human Injury and Treatment**

L.A. Young, SimQuest, San Diego, CA

7. Changes in Blood Levels of S100B and Corticosterone after Mild Traumatic Brain Injury (TBI) and Hemorrhagic Shock (HS) in Wistar Rats

Donna Sieckmann, PhD, Naval Medical Research Center, Silver Spring, MD

8. Prospective, Randomized, Double-Blind, Placebo Controlled Investigation Evaluating the Effects of Perioperative Administration of Gabapentin in Patients Undergoing Shoulder Arthroscopy with a Combination of General Anesthesia and Interscalene Nerve Block

> CDR Dennis Spence (NC) Department of Anesthesia Naval Medical Center San Diego, CA

9. A Descriptive Pilot Investigation Evaluating Physiological and Psychological Stress Measurements in Patients Presenting for Elective Surgical Procedures

CDR Dennis Spence (NC) Department of Anesthesia Naval Medical Center San Diego, CA

Is Exercise Induced Asthma Due To a Water Channel Problem? 10.

> Chan W. Park, MD FAAEM Department of Emergency Medicine Naval Medical Center Portsmouth

11. Use of Microarray to Examine Neurotoxic Potential of Middle Eastern Sand: Relevance to Exposed U.S. Military Troops

> Palur Gunasekar, PhD, Research Biologist, Naval Medical Research Unit Dayton, Wright Patterson Air Force Base, OH

Motor Performance of the Less Affected L Variability After Stroke

A.W. Dromerick^{1,2,3}, A.J. Metzger^{5,6}, P.S. Lum^{5,6}, R.

National Rehabilitation Hospital, Washington DC¹; Rehabilitation Medicine², Neurology Washington DC⁴, Center for Applied Biomechanics and Rehabilitation Research Catho

INTRODUCTION

*Intraindividual variability (IIV) has been demonstrated to be increased in brain disorders such as dementia, parkinsonism, traumatic brain injury.

Stroke typically causes motor impairments in the contralesional hemibody, but ilso causes subtle motor impairments in the ipsilesional side.

We investigated whether increased IIV in motor performance compared to controls was detectable using a grip task.

OBJECTIVE

To determine whether participants with first clinical stroke would have increased IIV on the dynamometer grip task compared to age matched controls.

METHODS

Study Design: This was a cross sectional study of stroke rehabilitation

·Subjects:

- •Had sustained either ischemic or hemorrhagic stroke
- Stroke rehabilitation inpatients
- •Were not participating in any other acute stroke intervention studies
- •Had either clinical demonstration or subjective complaint of upper extremity
- •Were able to provide informed consent and follow 2 step commands
- •Had no prior upper extremity impairments or limitations to their independence

Experimental Task Description:

- •An instrumented grip dynamometer (G100, Biometric Ltd, sampling frequency 1000Hz) collected data
- Custom software (MATLAB) presented feedback about current force and target ranges on a computer screen
- Participants were tested in a seated position and viewed visual feedback on a computer screen as they attempted to keep their grip
- strength on the dynamometer within a target range
 •Target range presented visually was between 5% of no
- •Scripted presentation of task with brief practice attempts to familiarize participant with task
- •Beginning with visual stimulus, effort sustained for 4 minutes with scripted encouragement

•Analysis:

We assessed IIV in several ways:

- Time: Seconds outside of target range
- 2. Force: Standard deviation of grip force
- Force x Time: Summed rectified arrefront
 Force x Time: Summed rectified error out
 Independent sampled t-tests were used to e
 Independent sampled totals. Receiver Open

RESULTS

•Participant Demographics: •Age:

- •10 40-49yrs
- *14 50-59yrs
- -6 70-70yrs
- •4 80-89vrs
- iender: 25 M, 21
- VA Type:
- *41 Ischemic
- verage days since CVA

•12.14 + 5.37



Stroke subjects were different in a variety of

in material and a principal principal and a second

2. Some had difficulty with initiation:



Some had variability increasing with time



4. Some made multiple errors:



imb to Estimate Intraindividual

E. Tractenberg^{3,4}

v³, Collaborative for Research on Outcomes and Metrics, Georgetown University, lic University, Washington DC⁵, National Rehabilitation Hospital, Washington DC⁶.

from own mean generated force de target range cimate average differences ting Characteristic (ROC) curves e four IIV definitions in terms of specificity) rates

ct performance (See below) was following features: ne target force immediately iter the consistency of their

in target level of force with little



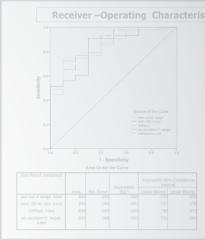
ways: ariable than controls

•Levene's test was significant (all p<0.01) for each of four IIV definitions, with patients demonstrating significantly higher variances on each of the four

variances on each of the four butcomes.

•The t-tests (not assuming equal variances), after correction for multiple comparisons (Bonferroni) were all also significant, with patients exhibiting

significantly greater variability o performance than controls



•The best performing summary (Int/Rect) has 85.3% of area under the curve (95% CI: 73.8% - 97.3%).
•The worst performing summary has 83.5% of area under the curve (95% CI: 70.2% - 96.7%).
•Thus, these four summaries of the dynamometry performance at intake discriminate similarly between patients.

DISCUSSION

IIV derived from a sustained submaximal ipsilesional grip task yielded statistically significant differences in stroke patients relative to controls.

For this grip task, different, definitions of IIV behaved similarly.

•The best performing summary of the grip task generated an 85% chance that a randomly chosen patient would be ranked as worse than a randomly chosen control.

•These data in persons with stroke demonstrate on the less affected side exhibit increased variability in grip force control compared to controls.

ADDITIONAL INFORMATION

Trial Name: : Motor Performance of the Less Affected Limb to Estimate
Intraindividual Variability After Stroke

PI/Coordinator Name(s): : Alexander W. Dromerick MD/Jill Terner BA PI/Coord. Affiliation(s): : National Rehabilitation Hospital/Georgetown

University/National Renabilitation Hospi

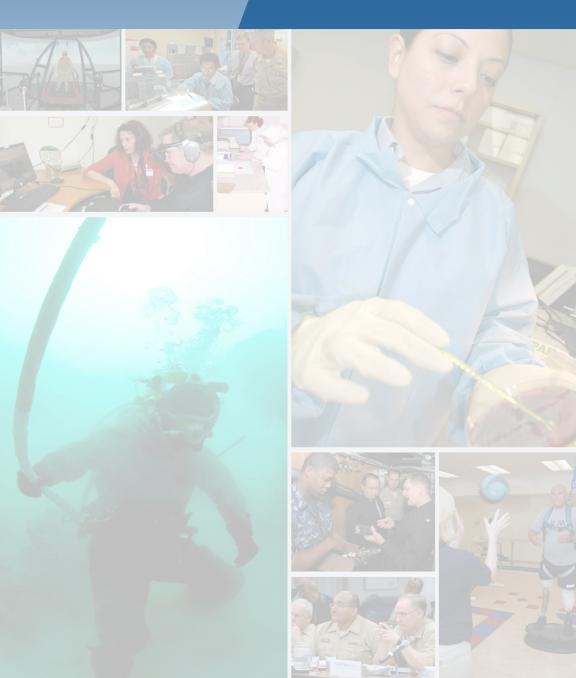








CONFERENCE OPENING





Navy Medicine Research and Development Conference Connecting Wounded Warriors to Advanced Diagnostic and Therapeutic Options Opening Keynote Address

Adam Robinson, Jr., MD

36th Surgeon General of the United States Navy c/o US Navy Bureau of Medicine and Surgery 2300 E Street NW Washington, DC, USA Tel: (202) 762-3701

Author Note

The opinions in this article are those of the author and do not represent the views of Navy Medicine, the Department of the Navy, the Department of Defense, or the United States Government.

Introduction

You know it takes a very special event to get me to put on my uniform on a Sunday. This conference is certainly one of them, and I am thrilled to be here. I very much appreciate the invitation to provide a Keynote for this meeting.

You all should know by now that I have made research and development one of my top priorities since I became Surgeon General, almost four years ago. Therefore this conference's topic of how we connect Wounded Warriors to more advanced diagnostic and therapeutic options is near and dear to my heart. I can think of no more important mission at Navy Medicine than taking care of our men and women in uniform who bear the seen and unseen wounds of war. The world class care we provide today is a direct result of the razor sharp focus we have placed on translational research advancements for our wounded warriors. This mission starts with each and every one of you in this room.

I thank all men and women involved in Navy Medicine research activities for what you do throughout the year to advance the quality of care we provide our Sailors, Marines, and their families. I also want to express how much I am thankful to the men and women around the world who are not with us, all of our brothers and sisters in harm's way who are doing the hard work of military medicine while deployed to far corners of our world and personally engaged in carrying out Our Nation's business.

I would also like to thank everyone who played a role in putting on this conference, and especially: Dr. Wayman Cheatham, my Special Assistant for Medical Research and the Director of the Navy Medicine Research and Development Center. Thank you for your leadership and your service. Also, Dr. Ken Green, Commander, Dental Corps, the Associate Director for Research Operations Integration at the Navy Medicine Research and Development Center. Thank you, Dr. Green, for organizing an outstanding Conference and

for all that you do. Thank you to the Uniformed Services University of the Health Sciences for hosting this event. And, last but not least, thank you and welcome to everyone here who has chosen a career in medicine in the service of others.

You are all doing what we have asked you do to: and that is to serve a cause larger than yourself; to serve with honor, courage, and commitment; and to serve with trust, integrity, and transparency. You truly are the best and brightest in military medicine. No matter how niched your activity may be, please know that the work you do is what makes it possible for us to succeed collectively. Even if at times you may feel isolated, your work is not only integral to the Enterprise mission, it has direct impact on our wounded warriors, from the battlefield to the bedside. I know that many of you have deployed as well. Therefore, I thank you all for the great work you do, and for your steadfast commitment to service.

My objective today is simply to highlight some of our recent accomplishments in Navy Medicine research and development and also tell you what our current challenges are and how we are meeting them

Importance of Translational Research Advancements

The quality of care we are providing our wounded warriors, in theater and throughout every level in the continuum of care, starts with what you all do in the research laboratories. And let me be clear about something. Research and Development is not important simply because of research funds. It is important because medical advancements start with an idea or experiment in a lab. As researchers and scientists, you all epitomize the spirit of interdisciplinary scholarship, innovation, and entrepreneurship. Science and technology, research and development are the bases from which most of our innovations originate. In fact, Navy Medicine would not be able to accomplish its mission without a vibrant research and development community. Many wounded warriors are walking, talking, and leading productive lives today because of your research and medical advancements. Research and Development programs are truly force multipliers.

As you know, we have ten medical research laboratories at home and overseas, focusing on programs as wide ranging as population-based medicine and epidemiology, aviation, undersea operations, directed energy, toxicology, emerging infectious disease evaluations, combat casualty care, diving medicine and many more. Due to the nature of wounds we have seen in Iraq and Afghanistan, our #1 research priority throughout my tenure has been Traumatic Brain Injury, from mild to severe, and psychological health treatment and support for both operational forces and home-based families. Our focused research has yielded tremendous results in combat casualty care in mild to severe TBI and post traumatic stress, as well as areas like wound management, wound repair and reconstruction, extremity and internal hemorrhage control, and phantom limb pain in amputees.

R&D Partnerships around the World

Our success in research stems from our overseas partnerships as well. We enjoy many diverse academic collaborations as well as more directly research-related partnerships with various nations. Our international colleagues come from many corners of the globe

including, for example, Egypt, Peru, Vietnam, Djibouti, Botswana, and others. In some of these, as we know, we house Navy Medicine research and development laboratories, and work directly in these with our host nation military medical counterparts. Our overseas laboratories provide superb research support. This research support applies to our over 500 civilian laboratory employees: 250 of whom are U.S. based, and 330 of whom represent foreign service national employees who assist our overseas laboratory network. After earning their advanced degrees, many foreign service national employees assume leadership roles in their homeland universities, and within the health, science and technology directorates within their governments.

Our three overseas laboratory commands and their subordinate detachments and field activities have enabled us to provide needed resources and diplomatic tools for the interagency to develop their own initiatives with foreign governments. Our signature method of providing "shoulder to shoulder" medical science, infectious disease and health hazard support to host nation governments has been repeatedly cited as their best practice model for building more trust, cooperation, and collaboration with us. To that end, we have held extensive international engagements and development relationships in Africa, South America and Southeast Asia-Pacific for over 66 years. Our extensive partnerships with military, civilian, and foreign contractor personnel, both at home and abroad, support our overseas operations and provide a much needed infrastructure for enhanced engagement.

This work directly supports our Nation's national security, diplomatic, and development strategies as well. Our engagement programs include partnerships in undersea and aerospace medicine, vaccine and infectious disease research, environmental health and toxicology, and surgical and reconstructive research, including regenerative medicine. Our forward presence overseas enables us to provide preparedness regarding potential threats infectious, toxic and environmental – existent on six continents.

These broad activities represent only a fraction of what Navy Medicine provides but they highlight our enhanced and enlarged global footprint of health diplomacy. These partnerships should serve as a model to grow and sustain our own capacity as well as the capacity of United States interagency programs for the future. Navy Medicine has a unique role to play in these missions because we transcend borders through our partnerships around the world. As global health diplomats and ambassadors, we are part of our Nation's Global Force for Good.

Current Challenges

So where are we challenged today in our ability to connect wounded warriors to advanced or emerging diagnostic and therapeutic options?

- Information asymmetry in Navy Medicine regarding the research occurring within DoD and in the civilian sector, especially with clinical trials;
- Lack of a process to systematically engage our patient population with various clinical trials; and,
- Existing barriers that impede universal access for all possible patients to available emerging therapeutic options;

As a possible solution to overcome these challenges we are looking closely at how we can better connect wounded warriors to options both within and outside of military medicine channels, while ensuring full compliance with patient safety policies and practices.

Progress to Date

Allow me to cover some of the areas where we are making tremendous progress:

- 1) We have aligned our Graduate Medical (GME-MR) and Allied Health Sciences (AHS-MR research opportunities with both SECDEF and SG Priorities)
 - a. This includes a host of supported research areas by clinical investigation programs at the MTFs, as well as active and completed Nursing Research and Allied Health Sciences research over the past 4 years, some of which have won awards.
 - b. Our Medical Corps and Nurse Corps have also won research awards at the final research award programs held a few weeks ago.
- 2) We have increased our financial support at Medical Centers to support medical research in two ways:
 - a. Through priority listing as GME-MR/AHS-MR research as fundable through usual DHP-O&M monies at Medical Centers; and,
 - b. Through the special direct research award program from my office and the Deputy Surgeon General's office at the Bureau of Medicine and Surgery.
- 3) We have developed a translational research project within the Navy Medicine Research and Development community to support collaboration with the clinical community fostered by Naval Medical Research Center, Silver Spring as the Research and Development Enterprise operational lead
- 4) We have realigned all Strategic and Policy Development and Exercise of Oversight of all Navy Medicine Medical Research Assets from within my office with reporting through the Regions directly to my office with day to day operational oversight by my Special Assistant.
- 5) We chartered the Navy Medicine Research and Development Center (NMRDC) within the Navy Medicine Institute to provide administrative alignment and support for the Bureau of Medicine and Surgery level Alignment of Strategy and Policy Development and Exercise of Oversight
- 6) We formed the Executive Research Advisory Board, composed of the following: the Flag Commanding Officers of the Regions (NAVMED East, NAVMED West, NAVMED NCA, NMSC); The Medical Officer of the Marine Corps; the Fleet Forces Command Surgeon; the Pacific Fleet Surgeon; the Surgeon General's Special Assistants and research-related program directors; the Commanding Officer of the Naval Medical Research Center; the NMRDC Deputy Director for Clinical/Medical Research; the NMRDC Deputy Director for Nursing and Allied Health Sciences Research; and the Commanding Officer of the National Intrepid Center of Excellence (NICoE), among others.

- 7) We formed the Emerging Therapeutics Panel for surveillance and review of ALL TECHNOLOGICAL AND CLINICAL intervention developments that are emerging world-wide and reported via Scientific and Medical publications, medical and scientific conferences, public media, subject matter experts
 - a. We are evaluating these developments through a select panel of experts from both within the Department of Defense and Navy Medicine, as well as from the academic and private technology communities who are rendering opinions on the advisability and route of access to these technologies for appropriately prepared wounded, ill and injured.

Therefore, as I have highlighted, we have made tremendous progress to date and we are poised to continue this record of progress and achievement in the coming months and years, with your help.

Conclusion

Although these accomplishments demonstrate progress, I pledge to you that, with your help, we will we never stop striving to ensure that Our Nation will always have a medically ready / fit / fighting force; and that those who have served Our Nation along with their families can always count on Navy Medicine and the entire Military Health System to provide quality and compassionate patient and family-centered healthcare, especially for our Wounded Warriors.

Ladies and Gentlemen, you are answering the call to service. The work you do is of great value and service of the highest order to our Nation and is very much appreciated and valued.

Please remember: what we do does not have to be complex or complicated. We simply need to step forward and do what is right. You do not ever have to ask permission to do what is right. That is what Honor, Courage, and Commitment are all about.

I was asked recently, what were the two most important things that I learned from the military and from medicine. And I was instantly able to say, I learned from the military the concept and the ethos of service. The ethos of Honor, Courage, and Commitment, the ethos that selfless service is something we must provide to every man and woman that we call Shipmate and anyone with whom we work. We are all shipmates and rise and fall with the tide together. Therefore, Service is incredibly important.

It has indeed been an honor and privilege to address such an important gathering of professionals.

God bless you all.

Thank you very much.

VADM Adam M. Robinson, Jr., MC, USN (Ret) 36th Surgeon General of the Navy and Chief of the Navy's Bureau of Medicine and Surgery

Between 2007 and 2011, Vice Admiral Robinson served as the 36th Surgeon General of the Navy and Chief of the Navy's Bureau of Medicine and Surgery. He is a native of Louisville, Kentucky. He entered the naval service in 1977 and holds a Doctor of Medicine degree from the Indiana University School of Medicine, Indianapolis, through the Armed Forces Health Professions Scholarship Program. Following completion of his surgical internship at Southern Illinois University School of Medicine, Springfield, he was commissioned.

His first assignment was as a general medical officer, Branch Medical Clinic, Fort Allen, Puerto Rico, before reporting to the National Naval Medical Center, Bethesda, Md., in 1978 to complete a residency in general surgery. His subsequent duty assignments included: staff surgeon, U.S. Naval Hospital, Yokosuka, Japan, and ship's surgeon, USS *Midway* (CV 41).

After completing a fellowship in colon and rectal surgery at Carle Foundation Hospital, University of Illinois School of Medicine Affiliated, Champaign-Urbana (1984–85), Dr. Robinson reported to the National Naval Medical Center, Bethesda, as the head of the Colon and Rectal Surgery Division. While there, he was called to temporary duty in 1987 as ship's surgeon in USS *John F. Kennedy* (CV 67) and in 1988 as ship's surgeon in USS *Coral Sea* (CV 43).

Dr. Robinson reported to Naval Medical Center Portsmouth, Va., in 1990 as the head of the General Surgery Department and director of General Surgery Residency Program. He was appointed acting medical director for the facility in 1994. While at Naval Medical Center Portsmouth, Robinson earned a Master's degree in Business Administration from the University of South Florida. In 1995, Dr. Robinson reported to the commander, Naval Surface Force, U.S. Atlantic Fleet, as the force medical officer serving in that capacity for two years. Following that assignment, he reported to Naval Hospital Jacksonville in 1997 as the executive officer. In January 1999, as Fleet Hospital Jacksonville commanding officer, Dr. Robinson commanded a detachment of the fleet hospital as a medical contingent to Joint Task Force Haiti (Operation *New Horizon/Uphold Democracy*).

In August 1999, Dr. Robinson reported to the Bureau of Medicine and Surgery (BUMED) as the director of Readiness and was selected as the principal director, Clinical and Program Policy in the Office of the Assistant Secretary of Defense for Health Affairs in September 2000, where he also served as the acting deputy assistant secretary of Defense for Health Affairs, Clinical and Program Policy. Dr. Robinson was assigned as commanding officer U.S. Naval Hospital Yokosuka from September 2001 to January 2004, after which he received assignment back to BUMED as deputy chief of BUMED for Medical Support Operations with additional duty as acting chief of the Medical Corps. In July 2004, he reported as commander, National Naval Medical Center, Bethesda, Md. He assumed the duties as commander, Navy Medicine National Capital Area Region in October 2005.

The author of numerous presentations and publications, Dr. Robinson holds fellowships in the American College of Surgeons and the American Society of Colon and Rectal Surgery. He is a member of the Le Societe Internationale de Chirurgie, the Society of Black Academic Surgeons, and the National Business School Scholastic Society, Beta Gamma Sigma.

He holds certification as a certified physician executive from the American College of Physician Executives. In December 2010, he was awarded the honorary degree of Doctor of Humane Letters by his alma mater, Indiana University.

Dr. Robinson's holds many distinguished personal decorations including the Distinguished Service Medal (two awards), Legion of Merit (two awards), Defense Meritorious Service Medal (two awards), Meritorious Service Medal (three awards), Navy Commendation Medal, Joint Service Achievement Medal, Navy Achievement Medal and various service and campaign awards.



To Investigate the Influence of Acute Vestil Brain Injury on Subsequent Ability to Suc Therapy Program and Remain

Gottshall KR, Comprehensive and Complex Cas

Abstract

Mild traumatic brain(mTBI) injury secondary to blast exposure is a significant operational issue and a rising international concern in modern society. This abstract describes the vestibular/usual/cognitive patterns seen in these patients before, after, and one year following vestibular physical became (VET) treatment.

The objective of this study is to investigate the relationship of vestibular/visual/cognitive tests and the computerized dynamic posturography sensory organization test and the ability to remain on active duty status in the US military following VPT rehabilitation.

Among or group on £2 blast patients were althoughout on who responded to Very out group on £2 blast patients were althoughout on year later for long term dolf or followed by the control of the contro

All baseline (income) test scores were compared to outcomes scores taken 12 weeks after completing VPT, and one year after completing VPT.

DVAT, target following, target acquisition, and perception time normalized within twelve weeks whereas GST did not normalize until after 12 weeks of vestibular physical therapy SOT function normalized in all patients and this normalization was maintained in long term follow-in:

This set of vestibular/visual/cognitive tests appear reasonable to establish initial status, and to evaluate progress associated with participation in VPT. At the current time we can show significant improvement/mornalization for target following and DVAT testings occess. GVS was the most likely score to deteriorate over time. One year after VPT treatment, some of the benefits of vestibular rehabilisation are not maintained in a subgroup of these patients. We describe the characteristics of this subgroup and conclude that maintenance thorapy or chalanced vestibular archibit like in impropriat a dispart in folial vestibular rehabilisation.

Introduction

Blunt and blast traumatic brain injury (TBI) is a common cause of vestibular disorders. ¹² TBI secondary to blast exposure is a significant operational issue and a rising international concern. Our Comprehensive Combat and Comptex Casualty Care (C5) vestibular team has experience evaluating and treating a large group of of patients with this brain injury pattern. ² Our group has described the various vestibular symptoms associated with TBI secondary to blunt and blast injury. ⁵³ Our experience has demonstrated that vestibular physical therapy (VPT) rehabilitation is a beneficial traument modality in this croup of patients. ⁵³

Methods

Four groups of mild blast TBI patients (Figure 1, Figure 2) were treated with VPT: 82 patients were included in the study. There were 79 males and 3 females. The average age was 24 years with a range of 19 to 34 years. The computerized dynamic posturography (CDP) sensory organization test (SOT), and motor control test (MCT) was administered. A vestibular-visual-cognitive testing was administered to the exertional. Post blast disequilibrium (PBD), and Post blast disequilibrium with vertige (PBDV) groups using the Neurocom in Vision Tunnel. The vestibular-visual-cognitive testing was performed in a darkened room with an effective viewing distance of 10 feet. The test battery included static visual accity, perception time, target acquisition, target following, dynamic visual acuity (DVA), and gaze stabilization tests (GST).

The VPT program consisted of exercise procedures that targeted the vestibulo-coular reflex (VOR), cervico-coular reflex (COR), depth perception (DP) somatosensory retraining (SS), and aerobic function.

Forty-selven mTBI in their war and an area and a few and

Figure 1

Blast Injury

Post Traumatic Exertional Dizziness 24%

Post Blast Disequilibrium with Vertigo 47%

> Post Blast Induced Disequilibrium

Figure 2

Four groups of blast TBI patients treated with VPT include benign positional vertigo (BPV), sertional, blast induced disequilibrium vith vertigo (PBDV), and blast induced disequilibrium with vertigo (PBDV).

Classification of Dizziness After Blast Associated TBI

Figure 3

Target following increased from 9 degrees per second pre VPT to 13 degrees per second post VPT.



bular Impairment Following Mild Traumatic cessfully Complete a Vestibular Physical on Active Duty One Year Later



ualty Care, Naval Medical Center, San Diego, CA

Figure 4

Horizontal target acquisition time dropped from 350 msec pre VPT to 260 msec post VPT, and vertical target acquisition time dropped from 360 msec pre VPT and to 280 msec post VPT.



Figure 5

Dynamic visual acuity (DVA) loss decreased from .33 logMAR right to .2 logMAR; .36 logMAR int to .2 logMAR; .28 logMAR, and down to .18 logMAR, and .27 logMAR up to .18 logMAR pro VPT to post

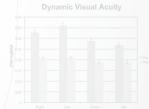
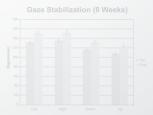


Figure 6

Horizontal GST left 140 degrees per second and right 144 degrees per second. Vertical GST down 136 degrees per second, and up 125 degrees per second pos VPT respectively.



Results

The CDP SOT test results of the four groups revealed a reduced vestibular profile for the PBD group with a mean score of 68, and the PBDV mean score of 68. This was in contrast to a mean score of 74 for the exertional dizziness group consistently that consistently met vestibular profile norms for the SOT test. The Motor Control feet (MCT) also revealed a significant higher percentage of prolonged translation atencies for the PBD and PBDV groups compared to the exertional dizziness group.

Noticeable improvement of perception time, target following, target acquisition, and DVA achieved expected standards after eight weeks of VPT. Group average perception time dropped from 43 msec to 27 msec. Target following increased from 9 degrees per second to 13 degrees per second (Figure 3). Horizontal target acquisition time dropped from 350 msec to 260 msec. and vertical target acquisition time dropped from 350 msec to 260 msec. (Figure 4). DVA logARA least accreased from 33 logARA? Right 12 260 msec. (Figure 4). DVA logARA? least accreased from 33 logARA? right to 2.0 logARA? right 1.3 flogARA? left to 2 logARA? Right 2.0 gas acquisition (GST) however did not return to standard level until completing an additional 4 weeks of VPT. Horizontal left GST of 140 degrees per second and right GST of 140 degrees per second with two additional weeks of treatment. Vertical GST of down 136 degrees per second own and 135 degrees up in estandards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees up met standards of 200 degrees per second own and 135 degrees per second

Objective vestibular testing of blast head injury in patients revealed that individuals with acute vestibular impairment following blast mTBI who did not stay on active duly and received an well-deal board displayed significantly lower pre-vestibular physical therapy Computerized dynamic posturography Adaptation Test scores. The same individuals displayed significantly prolonged time on the target acquisition saccade test. Computerized dynamic posturography MAptient ST, Computerized dynamic posturography MAptient Test, and Target Acquisition Saccade Test may represent a subset of fests may be used to predict the ability to remain on active duly twelve months after sustaining acute vestibular impairment following mid TBI from blast.

Conclusion

Visual-vestibular-cognitive tests are very sensitive measures of blast TBI verbular disorders. Pre-treatment test battery means of perception time, target following, target acquisition, DVA, and GST are highly accurate predictors of response to VPT. At the current time we can show significant improvement formalization for perception time, target acquisition, target following, and DVAT scores at 8 weeks of VPT. GST scores showed improvement for statistical significance in this blast TBI population after 12 weeks of VPT. The normalization of vertical GST paralleled the ability to run three miles and without vestibular symptoms during or upon cessation of the run.

Objective vestibular testing of blast head injury in patients injured in Iraq or Afghanistan is of value in predicting the ability to stay on active duty 12 months later. Predicting and influencing functional outcome following mild TBI in both our military service members and civilian patients remains a challenge to both the clinician and the researcher.

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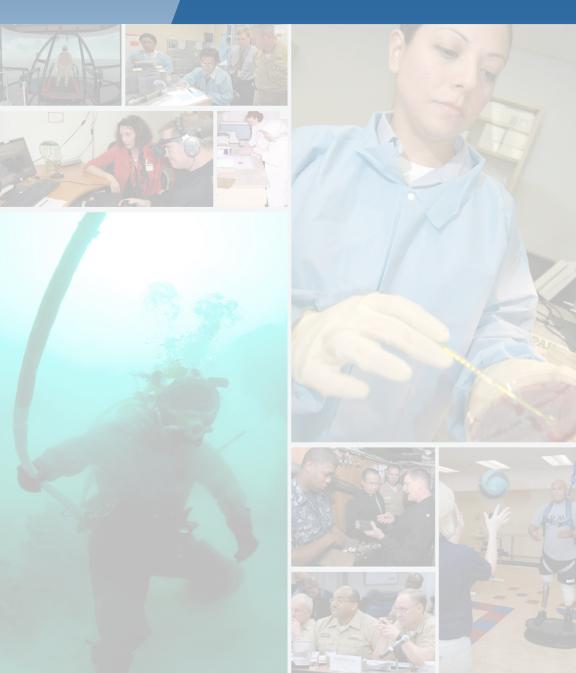
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The views expressed in this work are those of the authors and do not necessarily reflect the official policy



KEYNOTE SUMMARY MATERIALS





The texts found in the following pages were prepared by the conference's distinguished keynote speakers to summarize their respective lectures. These materials are lecture summaries designed to capture the major points of each presentation.

Navy Medicine Research and Development Conference Adipose Stem Cell Biology and Applications to **Wounded Warrior Care**

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Address

It is a great honor to be here today to talk about our efforts to develop new therapies for wounded warrior care. This effort is part of a major partnership between Department of Defense researchers and university researchers. This involves collaborations between research laboratories at many centers. Importantly, this is also a very strong collaboration between university physicians and active duty military surgeons who are treating the wounded warriors in the acute care setting.

Adipose tissue is a very rich source of mesenchymal stem cells, and this offers the promise of new therapies for reconstruction of traumatic wounds. These stem cells reside within adipose tissue and occur at much higher frequency per gram of tissue than bone marrow stem cells occur within bone marrow tissue. Additionally, adipose tissue is very easy to harvest through minimally invasive liposuction techniques with low risk.

The small stromal cells within adipose tissue demonstrate the properties of stem cells including: 1) self-renewal, or the ability to reproduce immature stem cells and replenish their supply; 2) asymmetric division, or the ability of certain daughter cells to mature while other daughter cells remain immature and; 3) pluropotency, or the capacity to differentiate into many different tissue types. Adult stem cells reside within most tissues of the human body throughout life and serve to turn over mature cells as they become senescent and lose their function. Adult stem cells live within a specific anatomic niche and are signaled to differentiate to mature cells during a process that is still not well understood. Once the stem cells are signaled to differentiate, they progress along a lineage-specific pathway toward a

specific phenotype. Most adult stem cells can be signaled to differentiate in culture using a defined culture medium containing specific growth factors in high concentration. Adult stem cells otherwise will tend to stay quiescent in the absence of strong chemical signals.

Stem cells can be separated from the fat tissue by first removing the fat tissue from the body by using a liposuction cannula. This results in small particles of adipose tissue measuring approximately 2–3 millimeters in diameter. This disaggregated adipose tissue is subjected to an enzymatic digestion to separate the stromal cells from adipocytes. The freshly isolated stromal cells are referred to as the stromal vascular fraction (SVF). This is a very mixed cell population containing multiple phenotypes with multiple combinations of cell surface markers. These include cells that display antigens such as CD34, CD31, and CD146, representing pericytes. These cells can be expanded in tissue culture through many passages and also cryo-preserved for future use.

In the laboratory, many different tissue types have derived from these adipose stem cells, including muscle, bone, cartilage, hepatocytes, and even cells resembling pancreatic islet cells that can secrete insulin and glucagon. This has created an interdisciplinary interest in this field of study as it is obvious there are multiple clinical targets across the human body. This is clearly demonstrated by the fact that a non-profit scientific society called the International Federation for Adipose Therapeutics and Science is now approaching its tenth year of existence (IFATS.org), and draws hundreds of people from around the globe for its annual meeting. This involves scientists from fields such as plastic surgery, developmental biology, cardiovascular biology, and neurosciences.

Adult stem cells can be used clinically under three general strategies. In the first strategy, the cells are introduced at the site of injury and will participate in the healing process through the release of growth factors. The cells may or may not assume the phenotype of the injured tissue. Many of the cell types within adipose stromal populations will release growth factors in very high concentrations under stressful conditions. Clinical and pre-clinical models using this strategy would include the introduction of adult stem cells into injured myocardium after ischemic injury or introduction of stem cells to the spinal cord after trauma. In this strategy, sub-populations of the stem cells may be purified and isolated, or a mixed population may be used. The second therapeutic strategy is a tissue engineering approach. In this approach the stem cells are induced to transform into a new tissue type for repair and restoration of damaged structures. The cells are often introduced with a biomaterial scaffold that regulates the microenvironment and provides mechanical support. This has been used clinically to regenerate bone tissue by a group in Finland. They published their results in human patients mixing adipose stem cells with a calcium scaffold to form new bone that was used successfully for reconstruction of the craniofacial skeleton. Our main focus using this tissue engineering approach is restoring soft tissue after traumatic injury in the craniofacial region and the extremities. A third therapeutic strategy is to use stem cells as a vehicle for gene therapy. This strategy is limited by safety issues related to viral transfection.

The use of adipose stem cells for tissue engineering of soft tissue is based on the ability of the cells to release growth factors that can increase the blood supply of regenerating tissue. This includes VEGF, which is up-regulated significantly under stressful conditions. Additionally, adipose stem cells can be differentiated to new adipocytes. A subpopulation characterized by

expression of CD34, with absence of CD31 expression, is highly prevalent within the adipose stromal population and has a tremendous capacity for adipogenic differentiation.

The reason we are pursuing this tissue engineering approach for craniofacial trauma is because there is an unmet need for precise shaping of facial features after severe trauma, especially blast injury. While we can reconstruct the bony skeleton of the face with some accuracy, it is the overlying soft tissue that gives the recognizable human appearance. As advanced as our current reconstructive techniques are, we still lack precision in shaping facial features to approximate a normal appearance. This is very important in allowing our wounded warriors to integrate back into society. Visible facial deformities can affect every aspect of a patients' life including all of their social relationships and employment opportunities. Our goal is to develop a minimally invasive technique for precise shaping of soft tissues of the face that is durable and safe. We believe that our understanding of adipose biology and the use of adipose stem cell technology will result in these types of therapies.

In designing therapies to create new adipose tissue at the site of injury, we take a progressive approach to technology development that starts with a search for existing technologies that can be modified to provide a foundation treatment strategy. In this case, we identified a technique of transferring fat tissue from one part of the body to another called autologous fat transfer, using hollow cannulas. While this technique has been used in the aesthetic surgical community, it has never been adapted for facial trauma. The limitation of this technology is the fact that a loss of graft volume over time, or resorption, has been observed in clinical cases although never well quantified.

Our first major clinical trial to establish minimally invasive therapy for facial trauma soft tissue reconstruction has been funded through a program of the Office of the Assistant Secretary of Defense for Health Affairs. This program is called the Biomedical Translational Initiative (BTI). The purpose of this program is to advance clinical therapies that can help improve wounded warrior care in the near term. In this program we are validating the use of autologous fat transfer for minimally invasive facial trauma reconstruction. This is possible through enabling technologies including specialized instrumentation that can apply the fat tissue in very tight anatomic spaces and can help release scar tethering. The technique is highly standardized and we have included a co-investigator on the team who is a pioneer in the techniques in fat grafting and who developed much of the instrumentation. This trial has a targeted enrollment of 20 subjects and 14 patients have been treated so far. All patients have gained a visible improvement in the appearance of their deformity and there have been no adverse events. The procedure is performed on an outpatient basis. We have assembled a team with broad expertise uniquely suited to this project, including expertise in plastic surgery, radiology and psychologists skilled in quality of life measures in wounded warriors. This study is still actively enrolling subjects and we welcome referrals. Under this program, all treatment expenses and travel expenses for our participating patients are covered, making this program accessible to anyone who meets eligibility criteria. Patients can participate if they have a visible deformity anywhere in the craniofacial region, including the skull.

In addition to assessing clinical outcomes as an end-point, basic science assays testing cell function and characterizing cells that are present in the adipose graft material are being preformed. It is our hope that we can correlate biologic properties of the graft

material with functional outcomes, and understand predictors of success with this procedure. The battery of assays includes flow cytometry of the isolated stromal cells within the graft material, as well behavior of the cells in culture and potential for differentiation.

The second phase of this study, also enrolling patients, is funded through a different but synergistic program in the Department of Defense called the Armed Forces Institute of Regenerative Medicine (AFIRM). While the first study provides baseline data and foundation infrastructure for the study of outcomes in minimally invasive facial reconstruction, the second study assesses a regenerative medicine component. The graft material is enriched with isolated adipose stromal cells from the same patient. Enriching the graft material may improve outcomes by capitalizing on the ability of these stromal cells to release growth factors and increase both the blood supply and the mass of the adipose tissue. We also welcome referrals for this study. The entrance criteria are the same, essentially enrolling patients who have a visible deformity in the craniofacial region. In both of these studies, patients are followed out through nine months with high-resolution CT scanning along with a battery of quality of life measures. Another component of this study currently going through the regulatory approval process will use adipose tissue grafting to treat amputation sites with poor soft tissue coverage. Many patients have the inability to fit a prosthesis because of pain and amputation sites and this may be a very valuable and helpful treatment option.

In summary, an understanding of adipose biology and adipose stem cell technology has the potential to result in approved reconstructive therapies for our wounded warriors. We are currently trialing new therapies in clinical studies that are currently available to wounded warriors at no cost to the patient because of Department of Defense support for this research. It has been a great privilege to have the opportunity to present at this meeting and to spend time with my colleagues in the military medical system. It is an even greater privilege to treat the wounded warriors who have participated in our clinical trials and to have a potential role in the development of therapies that my improve outcomes for wounded warrior care.

Thank you for your attention. I would be happy to answer any questions.

Navy Medicine Research and Development Conference

TBI and Neuroinflammation: A Rationale for Treatment: **Summary Text and Presentation Outline Notes**

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Introduction

An estimated 2-4 million people experience sport and recreation related concussions annually in the United States. (1,2) Additionally, the wars in Iraq and Afghanistan have resulted in 300 concussions per month—the greatest number and percent of mild traumatic brain injuries (mTBI) ever documented in a major war due to explosive devices as the opposition's weapon of choice. (3) Indeed, the diagnosis and management of concussions has become a healthcare crisis. (4) Four congressional committee hearings have been convened on the subject. Daily reports in the media document individuals with longterm disability from sports related concussions. In the military, it is now the most common cause of disability. (5-7)

The majority of the signs and the symptoms of cerebral concussion, such as headache, nausea, visual disturbance and balance abnormalities, spontaneously resolve within 2–7 days. (9) Substantial numbers, however, may experience prolonged and intractable headaches, memory impairment, cognitive abnormalities, depression, sleep disturbances and other symptoms that result in severe debilitation—the so–called post concussion syndrome (PCS). (8–13) These symptoms often result in significant disruption and even withdrawal from school, job or military activity.

Currently there are no objective biological measures to assess severity of the neuropathology following concussion. Loss of consciousness, formerly a hallmark of a concussion, occurs in only 10% of patients with PCS. (14) Neuro-imaging with CAT scans, MRIs, diffusion tensor imaging and PET scans have been less successful for predicting outcomes than was hoped. (15–18) Obviously, there must be disturbances in the neuropathophysiology and neurochemistry of the brain that go beyond observable structural changes that contributes to PCS.

Current management of the post concussion syndrome primarily involves rest and reduction of sensory input. But if rest and withdrawal from activities do not ameliorate post concussion signs and symptoms, pharmacologic agents are often prescribed. These treatments include anti-depressants, neurostimulants, hypnotics, analgesics, anxiolytics and possibly hormonal therapy, each with their own attendant risks and side effects.

This lecture discusses a new understanding of the pathophysiology of mTBI and, based on this newly proposed mechanism, new therapeutic treatments with generally fewer side effects for treating PCS. Specifically, we propose that PCS and the newly identified post mortem condition referred to as chronic traumatic encephalopathy (CTE), may both be due to mTBI activation of immune receptors (activated microglia) within the CNS and excitatory neurotransmitter release, referred to as an excitotoxic reaction. Termed as immunoexcitotoxicity, this concept may be the underlying basis for the neuro-inflammatory reaction that occurs in the traumatized brain. (19)

Unrelenting Media Coverage

The recent high profile sports related concussions and marked increase in IED blast related TBI and mTBI with the military, have placed a spotlight on the prevention, diagnosis and treatment of PCS. There have also been high level reviews of PCS from both government and military inquiries. Although significantly different mechanisms of injury, both contact sports and military blast related mTBI appear to have similar clinical and outcome results that may allow similar management and treatment strategies.

Definition of Concussion/mild TBI

Adopted by the Department of Defense and the Veterans Administration: "A blow or jolt to the head resulting in brief alteration in consciousness, loss of consciousness (lasting less than 30 minutes), or post-traumatic Amnesia"

mTBI (Concussions) in Sports

Contact sports – NFL, NHL, and high school football – have well over 1 million participants with an average concussion rate of 8.5%, 10.3% and 5.75%, respectively. The military's rate for recent deployments of over 1 million soldiers is 19%. (20-22)

Post Concussion Syndrome (PCS)

Symptoms may include:

- 1. Chronic headaches
- 2. Fatigue
- 3. Sleep difficulties
- 4. Personality changes (e.g. increased, irritability, emotionality)
- 5. Sensitivity to light or noise
- 6. Dizziness when standing quickly
- 7. Deficits in short-term memory, problem solving and general academic functioning

Military Post-Traumatic Stress Disorder

May have same or similar pathophysiologic mechanisms and symptom complex as PCS

Symptom Complex

- 1. Traumatic Event
- 2. "Flashbacks"
- 3. Avoidance
- 4. Hyper-responsiveness
- 5. Emotional Liability
- 6. Autonomic Reactivity
- 7. Sleep Disturbance

Incidence of PTSD

- 1. **Vietnam War 15%** men / **9%** of women, immediate (479,000) and ~30% men / 27% women lifetime (1 Mil)
- 2. Persian Gulf War veterans range from 9% to 24%
- 3. **Iraq War and Afghanistan** ~**12.5**% PTSD (23–29)

CTE-Chronic Traumatic Encephalopathy

In 2005 Omalu published post-mortem brain evaluations of numerous professional football players who had pathologic brain cellular changes similar to Alzheimer's tau deposits. Described as chronic traumatic encephalopathy, Omalu, et al, concluded that these changes were related to mTBI, both symptomatic and also described as "sub-concussive blows to the head." Several others have also found similar pathologic findings in a wide variety of sports athletes, including McKee et al, in 2009. (30–31)

CTE-Chronic Traumatic Encephalopathy—The New Agent Orange

- 1. Sub-concussive blows
- 2. Prolonged latent period
- 3. Mean survival of 18 years after diagnosis
- 4. Early behavioral personality changes with memory loss
- 5. Progressive dementia, Parkinsonism, gait and speech disorders

CTE-Questions Remain

- 1. How to diagnose?
- 2. How to treat?
- 3. How to prevent?
- 4. What is the actual prevalence?
 - a. (minimum—3.2% of retired NFL players?)
- 5. What are the risk factors?
 - a. Genetic (Apo E4)
 - b. Severity of trauma
 - c. Type of trauma
 - d. Frequency and time interval between successive head injuries
 - e. Age of individual at time of injury
 - f. Positive played and type of sport

Evolution of Inflammatory Immune System Known Neurological Conditions Associated with Cerebral Inflammation

Theories as to the underlying mechanism of CTE and mTBI have recently centered on the inflammatory process. Brain Inflammation from mTBI may activate Immuno-excitotoxicity through Microglia activation. (19)

- 1. Micoglia are Resident Macrophages of CNS
- 2. Primary Active Immune Defense CNS
- 3. 20% of Total Glial Cells
- 4. Pro-inflammatory Neuro-inflammation
 - a. Cytokines IL-1a, IL-1B, IL-6, TNF-a
 - b. Chemokines MCP-1
 - c. Proteases Cathepsins, MMP
 - d. Amyloid Precursor Protein APP
 - e. Inflammatory Prostaglandins PG-1, PG-6

Immunoexcitotoxicity as a Central Mechanism in Chronic Traumatic Encephalopathy—A Unifying Hypothesis

Proposed and published by Russell Blaylock and Joseph C. Maroon in Surgical Neurology International in July 2011, this is the theory of how mTBI can potentially lead to both PCS and CTE and perhaps PTSD. Immune overactivation via activated microglia and excitotoxicity from excessive levels of neurotransmitters may lead to a chronic inflammatory condition in the brain. This excessive inflammation may lead to chronic and prolonged PCS, PTSD and the destructive brain changes seen in CTE. (19)

Concussion-Acute Cellular Inflammation

- 1. mTBI causes a Transient Release of high levels of
 - a. ROS/RNS
 - b. lipid peroxidation products
 - c. Prostaglandins
 - d. nitric oxide
 - e. neurotransmitters
- 2. All can then activate microglia
- 3. Activation of Microglia Macrophage will stimulate
 - a. Immune mediated Inflammation
 - b. Genetic upregulation of chemokines
 - c. tumor necrosis factor alpha (TNF)
 - d. NFK-B
- 4. Typically Acute Inflammation response will abate and healing will occur

Unanswered Questions about CTE and Immunoexcitotoxicity

- 1. What are the Risk Factors?
 - a. Prior "Priming" of Microglia Cells?
 - b. Severity and Frequency of Trauma?
 - c. Age?
 - d. Genetics (ApoE4)?
- 2. How to Diagnosis?
- 3. How to Treat?
- 4. How to Prevent?
- 5. What is the True Incidence?

Diagnosis and Treatment of PCS

ImPACT[™] is the leading neurocognitive system available for concussion testing. With over 2 million tests completed, used by most professional sports teams, over 3,000 colleges, universities and high schools around the world. (www.impacttest.com)

- 1. Independently validated with proven sensitivity and specificity
- 2. Correlated with fMRI
- 3. Can be scaled to test millions of people
- 4. Optimized and proven security
- 5. Positive response from military users
- 6. Customized to military specifications

Current Treatment Standards for PCS

Pharmacological

- 1. Anti-depressants
- 2. Hypnotics
- 3. Anxiolytics
- 4. ADHD meds

Rest the Brain (no brain stimulation)

1. No work, school, TV, etc

Proposed Treatments for PCS

Anti-Inflammatory-

COX inhibitors—(Pharmacologic-Aspirin, Ibuprofen, Celecoxib, Naproxen, Natural-Fish Oil, Resveratrol, Quercetin, Curcumin, Green Tea, Hyperbaric Oxygen) Block Cytokines, and Microglia-(Pharmacologic-Minocycline, Progesterone Natural-Fish Oil, Resveratrol, Curcumin, Vitamin D, Magnesium, Luteolin, Hyperbaric Oxygen)

Enhance Brain Function-

(Increase BDNF-SSRI's, Tricyclics, ECT Progesterone, Fish oil, Resveratrol, Curcumin, Exercise, Hyperbaric Oxygen

Enhance Immune Function-

Probiotics, Vitamin D, b-Glucan, Exercise Hyperbaric Oxygen

Activate Sirt1-

Resveratrol, Quercetin, Fish Oil, Curcumin, Green Tea, Hyperbaric Oxygen

Beneficial Supplements

Omega-3 DHA

Neurogenesis

Anti-oxidant

Membrane building

Protect from

Excitotoxicity

Inflammation

"Dietary Supplementation with the Omega-3 Fatty Acid Docosahexaenoic Acid in Traumatic Brain Injury," Bailes et al Neurosurgery. 2011 Jan 5 (31)

"Omega-3 DHA and EPA shown to reduce oxidative damage, counteract learning disability and normalize BDNF-J Neurotrauma. 2008 Dec; 25(12):1499.

"Omega-3 fatty acids that ameliorate protein oxidation the reduction of the energy status of cells. Hippocampal levels of total and phosphorylated AMPK were reduced after TBI and levels were normalized by omega-3 fatty acts supplements." Wu A, Ying Z, Gomez-Pinilla F J Neurotrauma. 2007 Oct; 24(10):1587–95.

Resveratrol—The brain is highly susceptible to free radical damage, but Resveratrol (found in grape skins and seeds) acts as an anti-oxidant and neuroprotectant. Resveratrol prevents apoptotic neuronal death and, by suppressing FOXO proteins promotes neuronal survival. Resveratrol activates transcription factor SIRT1, which can inhibit NF- B signaling and reduce inflammation. (32)

Resveratrol Neuroprotection Potential Mechanisms:

Anti-oxidant Blocks Free Radicals

Anti-Inflammatory Blocks NFkB Increases NO Vasodilatation

Anti-platelet Decreased Clotting
Anti-apoptosis Decrease Infarct Size

Other Potential Treatments

Hyperbaric oxygen using 100% oxygen at 1.5 ATM has been tried in a number of case report studies and shown improvements in both chronic PCS and PTSD. The underlying mechanism is believed to be anti-inflammation, thereby suppressing the immunoexcitotoxic response. Larger randomized trials have recently been funded by the military. (34)

Conclusion

The recognition and incidence of cerebral concussion continue to increase in sports, the military and in the general population. The anatomical consequences to brain structure and the pathophysiological changes (PCS and CTE) that can occur following TBI have recently garnered immense public awareness.

Microglial activation and immunoexcitotoxicity are believed to be major components in the etiology of the prolonged and often disabling symptoms of PCS and provide an underlying substrate for the biochemical and immunological events that take place in the concussed brain. This concept may be just one part of a cascade of additional pathophysiological events that simultaneously occur.

Based on the proposed inflammatory mechanisms of PCS and possibly PTSD a select number of natural anti-inflammatories are proposed as effective treatments to reduce the inflammatory response following mTBI, support neuronal function and healing and counter key mechanisms associated with post traumatic immunoexcitotoxicity.

Additionally, case reports suggest that HBO, through its anti-inflammatory action, may be another therapeutic option for the treatment of PCS and PTSD.

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Navy Medicine Research and Development Conference

Immune Modulation for Hand Transplantation: Changing the Risk-Benefit Balance

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Author Note

This text summarizes the material from one of the distinguished keynote presentations for the 2011 Navy Medicine Research and Development Conference. The opinions in this article are those of the authors and do not represent the views of Navy Medicine, the Department of the Navy, the Department of Defense, or the United States Government. This work was funded in part by the Armed Forces Institute for Regenerative Medicine (AFIRM) W81XWH-08-2-0032, Orthopedic Extremity Trauma Research Program (OETRP) W81XWH-08-1-0421 and the University of Pittsburgh Medical Center. The authors declare no conflict of interest.

Introduction

Millions of individuals each year sustain injuries, have tumors surgically excised or are born with congenital defects that require complex reconstructive surgeries to repair the resulting large tissue defect (1). In addition, devastating combat-related craniofacial and extremity injuries often result in severe tissue loss due to limitations of body armor (2, 3). The functional limitation of such injuries leads to significant impairment of mobility, stamina and agility and frequently prevents service members from returning to duty, compromising years of training and expertise.

It is the prime mandate of Plastic and Reconstructive Surgery, through a combination of technique and technology, ever since its initiation as a medical specialty, to restore such devastating tissue defects and to replace "like-with-like" tissue. However, current conventional reconstructive procedures often suffer from poor functional and aesthetic outcomes requiring multiple revision procedures, prolonged rehabilitation, multiple surgeries or hospitalizations, and site morbidity resulting from use of autologous tissues.

The use of composite tissue allografts is one promising solution to the overwhelming need for tissue for reconstruction, allowing the surgeon to replace "like-withlike" and to restore the appearance, anatomy and function. Over the past decade, vascularized composite allotransplantation (VCA) such as hand and face transplantation has become a clinical reality and a viable treatment option for those wounded warriors and civilian patients in need who suffer from complex tissue injuries or defects not amenable to conventional reconstruction.

Despite the fact that early and intermediate functional outcomes are highly encouraging, rejection and the need for toxic high-dose multi-drug immunosuppressive treatment continues to be the bane of VCA preventing wider clinical application. Thus, any reconstructive measures to improve these non-life threatening conditions must address a delicate balance of risks and benefits.

The Problem of Immunosuppression

Currently, broad and routine clinical use of VCA to restore devastating extremity injuries is hampered by the risks and toxicities of chronic high-dose conventional immunosuppressive medication required for graft survival (4, 5). Major side effects of such protocols include bacterial and viral infection, metabolic problems and malignancy. Thus, these risks greatly compromise recipient quality of life and jeopardize the potential benefits of reconstructive transplantation such as regaining form, function and independence. Considering the collective risk of the aforementioned complications, lifelong immunosuppression can be considered as a chronic disease that is characterized by its own set of risks.

When extrapolating from previous experience with solid-organ transplantation, chronic high-dose triple-drug immunosuppression may predispose a hand/forearm transplant recipient to an 80% chance of developing an infection (minor and/or major bacterial or viral), a 20% potential risk of developing post-transplant diabetes or renal failure, and a 4% to 18% potential risk of developing a malignancy in particular post-transplant

lymphoproliferative disease (PTLD). Such adverse effects unequivocally alter and impair the benefits of a quality-of-life enhancing procedure such as hand/forearm transplantation.

Recently, various modifications have been applied to the immunosuppressive protocols used in hand transplantation such as steroid sparing/avoidance attempts, conversion from tracrolimus to the mTOR inhibitor sirolimus for long-term therapy or the use of topical steroid and tacrolimus ointments to reduce the overall amount of systemic immunosuppression. Although great strides in these regimens have been made, the side effects and complications related to chronic multi-drug immunosuppression after hand transplantation remain considerable (4). In addition, chronic multi-drug immunosuppression is expensive and causes substantial long-term costs. Furthermore, due to the amount of daily oral medication required and its resulting high patient burden such regimens frequently lead to non-compliance. However, considering these obvious down sides of multi-drug immunosuppression and its various, sometimes severe side effects there is an evident need for novel concepts of systemic immunosuppression in reconstructive transplantation.

Maintaining graft survival while reducing/minimizing adverse effects and improving or optimizing functional outcomes stands to significantly impact the risk-benefit equation of such procedures enabling their widespread application as a novel reconstructive treatment option for both wounded warriors and civilian patients alike.

A Novel Treatment Protocol for Reconstructive Transplantation

As proposed by Drs. Starzl and Zinkernagel in their seminal 2001 article, two immunologic responses occur following organ or tissue transplantation: the *host-versus-graft* response driven by host effector cells and a *graft-versus-host* response caused by "passenger" leucocytes which are delivered together with the graft (6). If these two activities are not reciprocal and balanced, one cell population will predominate over the other resulting in either graft rejection or graft versus host disease (GvHD).

Spontaneous tolerance, achieved in experimental organ transplant models, is the result of an exhausted host-versus-graft immune response. Such a state of operational tolerance is achieved when the immune response towards the transplant is exhausted because the specific cell clones mediating rejection are deleted. Furthermore, maintenance of engraftment is facilitated when a small number of donor leukocytes persist in the recipient (microchimerism) long-term (7, 8).

Immunosuppression-aided tolerance can occur in organ transplant models in which the recipient's immune response is reduced to a level that can be controlled with a transient immunosuppressive / modulatory treatment using a single agent. Such a regimen requires depletional induction therapy in order to prevent an initial overwhelming immune response (9). However, the penalty of too little immunosuppression during the critical early post-transplant period may be irreversible rejection. Excessive prophylactic over-immunosuppression after transplantation on the other hand abrogates the previously described mechanism of clonal exhaustion and deletion. In such a scenario, the ineffectively deleted clone will reject the graft whenever immunosuppression is reduced. Thus, the initially over-treated recipient may then be committed to unnecessarily high maintenance immunosuppression (9).

The only chance to establish a balance between host and donor immune response selectively favoring tolerance is in the first few weeks after transplantation. During this time, the high degree of donor leukocyte migration provides the conditions for reciprocal exhaustion-deletion of donor-reactive recipient lymphocytes. A protocol, aiming to achieve such a state favoring tolerance, employing a strategy of providing optimal conditions for this to occur was proposed by Starzl in his 2001 paper. The concept involves a depletional antibody infusion before transplantation that reduces but does not abrogate the anti-donor immune response but allows maintenance treatment with tacrolimus to prevent rejection. Subsequently, low-dose monotherapy with tacrolimus to preserve naturally occurring mechanisms of clonal exhaustion / deletion leads to a state of immunomodulation or operational tolerance in the recipient. The additional donor bone marrow cell therapy enables donor-antigen specific immunomodulation by facilitating a constant source of donor antigen thus allowing a sustained interaction between the recipient and donor immune cells. Such a concept stimulates intrinsic mechanisms such as clonal exhaustion and deletion and finally immune ignorance to terminate the adaptive immune response and restore the quiescent state of alloreactive recipient lymphocytes.

This novel immunological paradigm was translated into a clinical protocol resulting in the first series of patients transplanted with a solid organ (kidney or liver) with or without very low levels of maintenance immunosuppression (10, 11). The application of such an immunomodulatory concept is particularly appealing in reconstructive transplantation due to several reasons.

- The skin component of a hand allograft can be easily and continuously monitored for early signs of acute rejection.
- II) The skin offers the possibility of transdermal (topical) drug application and delivery as an alternative to increasing systemic treatment.
- III) Skin biopsies can be easily taken per protocol as well as whenever clinically indicated. Not only is the morbidity minimal but also the sensitivity of detecting rejection is optimized as biopsies can be taken exactly from a lesion. Therefore, immunosuppressive therapy can be continuously adjusted to the clinical situation without the risk of missing rejection.
- IV) Composite tissue grafts contain immune-competent elements such as bone marrow (BM) and lymph nodes that may hasten the rejection process. Some certain types of hand and upper extremity transplants, depending on the primary defect, include BM and might thereby function as a vascularized bone marrow transplant by itself. Such a graft represents a continuous source of donor cells, including BM-derived dendritic cells, which have been demonstrated in animal models to favorably modulate the host immune response (12).
- V) In addition to being able to visually assess the graft, specific assays for immune monitoring allow to assess immunoquiescence and provide guidance in the clinical decision making process of tapering/weaning off immunosuppressive medication.

Thus novel strategies to minimize immunosuppression or even to achieve the ultimate attainable clinical goal of transplantation to induce immune tolerance are particularly promising in reconstructive transplantation.

Preliminary Data in Reconstructive Transplantation

Studies from our own group and laboratory furthermore demonstrated that a composite tissue allograft elicits a less intense alloimmune response than did allografts of each of its individual components thereby challenging the relative scale of tissue antigenicity (13). Using the by Starzl proposed immunomodulatory concept of pre-transplant lymphocyte depletion followed by low-dose tacrolimus monotherapy and donor BM augmentation in a complete MHC-mismatched swine heterotopic hind-limb transplant model we were recently able to achieve indefinite graft survival without the need for long-term systemic immunosuppressive treatment (14). Underlying mechanisms that have been identified include, for example, effects such as macro and micro-chimerism, and exhaustion and deletion of the recipient's T cell clones as outlined above. These insights helped to refine the treatment protocol aiming to support long-term graft survival on minimal maintenance immunosuppression in reconstructive transplantation.

Based on this novel paradigm in transplant immunology and on the data obtained in our laboratory in small and large animal models we implemented this BM cell based immunomoduatory protocol for the first time in human reconstructive transplantation (15). Five patients received between March 2009 and September 2010 a total of eight hand/ forearm transplants [bilateral hand (n=2), a bilateral hand/forearm (n=1) or a unilateral (n=2) hand transplant]. Patient I: Is a 24 year-old Marine who lost his right, dominant hand due to a blast injury in a training exercise and received a right hand transplant at the distal forearm level. Patient II: Is a 57 year-old Air Force veteran with bilateral mid-forearm and lower limb amputations due to Streptococcus A sepsis who became the first US bilateral hand/ forearm transplant recipient. Patient III: A 41 year-old National Guardsman received the first US above-elbow (right) and hand transplant (left) after loss of limbs in a farming accident. Patient IV: Is a 25 year-old female with quadruple limb amputation due to Norovirus sepsis receiving a right distal-forearm level hand transplant. Patient V: Is a 33 year-old female quadruple amputee due to meningococcal sepsis underwent bilateral distal-forearm level hand transplantation. Currently, 4/5 patients are maintained on a single immunosuppressive drug (tacrolimus) at low levels and continue to have increased motor and sensory function of their transplanted hands. Patients demonstrate sustained improvements in motor function and sensory return correlating with the time after transplantation, level of amputation and participation in hand therapy. Episodes of skin rejection were few and responsive to topical therapy alone or short courses of steroids. Overall, the side effects of immunosuppression were mild and transient without occurrence of any systemic infectious complications.

These initial and emerging data suggest that the protocol is safe, efficacious and well tolerated and that it allows reconstructive transplantation in upper extremity amputees with low-dose tacrolimus monotherapy while minimizing cumulative risks of immunosuppression.

Conclusion

Despite initial skepticism and debate, hand/forearm transplantation is a clinical reality. The development of novel cell-based immunomodulatory regimens that integrate the concepts of immune regulation with those of nerve regeneration to minimize/avoid immunosuppressive medication and to enhance functional outcomes will improve the safety, clinical success and life enhancing benefits of these reconstructive modalities and significantly favor the risk to benefit equation. This could not only usher in a new era in VCA towards broad and routine application but also will ultimately enable injured warfighters and civilian patients to regain their identity and integrity and reintegrate into social life and normalcy.

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Use of Microarray to Examine Neuroto Relevance to Expose

Krishnan Prabhakaran, Michael

NAVAL MEDICAL RESEARCH UNIT AT DAYTON (NAMRU-D) ENVIRONM

ABSTRACT

Introduction: Military personnel deployed to the Middle East have concerns regarding exposure to elevated levels of dust generated from blowing desert sand. Results from the Millennium Cohort Study substantiate these respiratory health concerns. Metals and harmful chemical components present in Middle Eastern sand have been identified as contributing factors for toxicity. Recent work in our lab has shown that soluble components of Afghanistan sand can be toxic and leads to apoptosis in a neuronal cell culture model. However, the exact mechanism of sand toxicity has not yet been identified. Objective: To evaluate particulate matter (PM)-induced neurotoxicity using microarray technology and to investigate whether sand-dust induced neurotoxicity using microarray technology and to investigate whether sand-dust induced neurotoxicity could alter the expression of apoptotic genes related to cell death pathways in correlation with cytotoxicity. Methods: Neuronal cells (MES 23.5) were exposed to different concentrations of soluble sand extracts (100 and 500 mg) and Microarray analysis of gene expression was carried out using the Affymetrix GeneChip System. Results: Gene Ontology analysis identified over 100 candidate genes which were significantly related to cell cycle and apoptosis, in particular Endoplasmic Reticulum and mitochondrial stress related, and glutathione metabolic pathways, which may be involved in cellular cytotoxic response to sand exposure. The changes in differential gene expression observed indicate exposure to sand significantly alter normal gene expression patterns. Conclusion: Overall, the changes in gene expression in neuronal cell culture following exposure to sand not only indicate a cellular stress response, but also decreased cell cycle progression and cellular in armia poptotic process and protein transcription. It is suggested that alterations in normal cellular biology, like those observed, may lead to changes in health in our troops exposed to sand dust; however, this warrants further inve

BACKGROUND

U.S. military personnel deployed to the Middle East in support of Operation Iraqi Freedor and Operation Enduring Freedom have concerns regarding exposure to elevated levels of dust generated from blowing desert sand (Englehardt et al, 2008; Bowman, 2004). It is known that airborne particulate matter (PM) exposure causes serious respiratory an cardiovascular health problems among deployed troops. Number of harmful metals an chemical components present in the sand dust (Lyles et al., 2008; Perdue et al., 1992) mabe inhaled and enter into extra pulmonary organs like brain in the body either b disturbing blood brain barrier or olfactory nerve transportation. PM can reach the brai where it can induce changes in neurotransmitter levels and pro-inflammatory cytokine and chemokines (Tin-Win-Shwe et al., 2008). Naval Medical Research Unit at Dayto (NAMRU-D) is interested to study the neurotoxicity due to Middle East sand inhalation b military personnel. Recent work from this lab has shown that soluble components of Afghanistan sand can be toxic and leads to apoptosis in a neuronal cell culture model. I order to understand the mechanism of toxicity, NAMRU-D further evaluated PM-induce neurotoxicity using microarray technology and investigated gene expression change related to toxicity in neuronal cells.

MATERIALS & METHODS

Rat Gene Array 1.0 microarrays were performed using RNA samples isolated from three biological replicates for each treatment condition (100 mg 6, 12, or 24 hours, 500 mg 6, 12, or 24 hours or vehicle treated control).

RNA isolation: RNA was extracted using E.Z.N.A Total RNA kits (Omega BioTek) and the manufacture's recommended protocol. Each RNA sample was subjected to Dnase treatment using TurboDNA Free (Ambion), RNA quality was determined by microfluidic analysis using Agilent 2100 Bioanalyzer and RNA 6000 Nano assays (Agilent) to ascertain that the RNA was of sufficient quality for further analysis. RNA integrity (RIN) numbers were all 10.0. A Whole Transcript (WT) Expression Array kit (Ambion) was used to generate biotinylated sense strand DNA targets from the isolated RNA as described in the kit protocol.

DNA quality and quantity was analyzed by nanand subjected to fragmentation and labeling a labeling kit (Affymetrix). Each sample was I washing, staining and scanning on the Fluidic protocol FS450-0007.

Array results were analyzed for differential gensamples. AltAnalyze (Emig et al., 2010) asses: filtering out probe sets with a Detection Above 0.05 and probesets with a non-log expression Is was applied to eliminate false positives (Benja filters and had a minimum absolute fold-change Elite (Salomonis et al., 2010), to determine over-r

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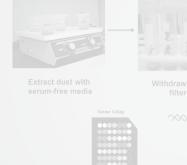


Fig. 1 (a): Genes Changed at 100mg Sand Exposure



This work was supported by Def

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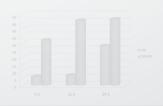
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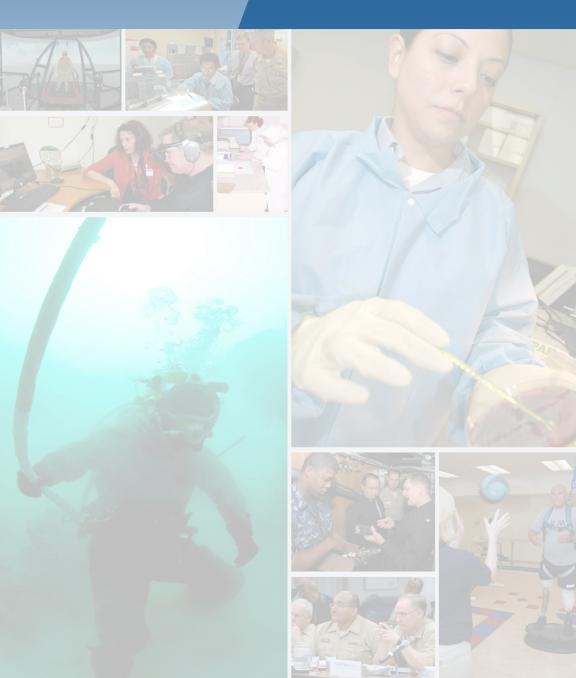








PRESENTATION ABSTRACTS





Repeated Exposure to Low Level Blast Overpressure Produces Impairment in Acquisition of Spatial Information

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Research Priorities and Gaps: Traumatic Brain Injury from exposure to IEDs.

Abstract

Exposure to improvised explosive devices (IEDs) in military personnel has resulted in a substantial increase in reported cases of mild traumatic brain injury (mTBI). This outcome has fueled a requirement to elucidate the effects of acute and repeated exposure to blast overpressure (BOP), one component of IEDs, which may play a causal role in the manifestation of cognitive impairment, particularly impairment of attentional mechanisms and working memory. We have previously demonstrated (Ahlers et al., 2008) that exposure to BOP produces impairment of memory and gross motor behavior related to the degree of blast intensity. Acute impairment was noted after a single exposure to 75 and 120 kPa; 120 kPa exposures were associated with overt brain, lung pathology and alteration of consciousness (AOC) whereas exposure to 75 kPa manifested none of these outcomes. No acute neuropathological or neurofunctional deficits were detected after single exposure to 40 kPa BOP. Having characterized the acute effects, we turned our attention to the analysis of repeated exposure to low-intensity levels of BOP that were not associated with overt pathological outcomes. Anesthetized adult male rats were repeatedly exposed to either lateral or frontal 40 kPa BOP, once per day for 12 consecutive days. Cognitive abilities were assessed in a Morris water maze (MWM) task 24 hours after the last BOP exposure. Results showed that repeated exposure to frontal BOP produced significant spatial learning deficits in the MWM task. In contrast, repeated exposure to lateral BOP did not produce significant cognitive dysfunction in this task. Collectively, these data suggest that cognitive abilities more closely associated with frontal lobe circuitry (i.e. attention, decision-making, working memory) may be more sensitive to repeated exposure to lowintensity levels of BOP. Implications of these data are discussed in relation to the manifestation of mTBI in military personnel exposed to repeated blast.

Support: Office of Naval Research: 0601153N.0000.000A0702 to STA.

A Digital Cranium Model for Prediction of Functional Deficits in Traumatic Brain Injury

Authors and Affiliations

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TASC, Inc.

Research Priorities and Gaps: Traumatic brain injury. Mitigation and treatment of neurotrauma.

Abstract

Blast-induced traumatic brain injury (TBI) has lead to development a number of finite-element models (FEM) and simulations designed to simulate expected stresses and strains in cranial tissues. TASC sponsored internal R&D to extend TBI modelling by constructing a fused, structural-functional data model of the cranium. This model has data structures that hold an overarching representation of the brain that maps the finite element representation (populated with tissue properties from the literature) to the Talairach coordinates and associated functional sites in the brain. A 1.8-million element cranial model was developed using SimpleWare® software to produce a 5-tissue (grey matter, white matter, CSF, skull, flesh) FEM from the BrainWeb® MRI brain image database of the Montreal Technological Institute. Using LS-DYNA as a multiphysics simulation environment, IED blast loads (shear stresses and strains) to the brain were simulated to predict dynamic changes in physical properties of the internal cranium. Blast loads (intensity versus time) are dynamically visualized and color-coded. Using Solid Works and other prototyping tools, we scanned and generated 3-D models of physical helmets, such as the Advanced Combat Helmet, so that blast loads across the cranium could be calculated with and without protection. One interesting result occurred when Brodmann Area 22 showed high strain with a helmet but lower strain without a helmet. Our model can estimate where blast loads are highest in the brain for different IED exposures, so it may be valuable for diagnosis, evaluating treatment strategies and designing improved protection. We are extending this corporate research into development of a 1st order ocular trauma model to better understand non-penetrating eye injuries.

Analysis of Navy-Marine Corps En Route Care (ERC) in OIF and OEF

Authors and Affiliations

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations. Wound / Injury Management Throughout the Continuum of Care. Advanced forward care.

Abstract

Background: En Route Care (ERC) has been provided by Navy nurses for critically injured casualties in OIF and OEF since 2001. Joint (JECC) and Navy (NERC) En Route Care Courses exist to train nurses, but no data have been published that document what types of interventions are performed during ERC, or whether these interventions are effective in maintaining or stabilising transported patients. This study represents the first ever objective data-based report of Navy ERC in OIF or OEF. Methods: Retrospective database review of medevac and ERC flights from two Marine Corps Echelon II to higher Echelon III facilities in Iraq (February 2005–March 2006) and Afghanistan (July-November 2009). Results: Of 1551 casualties treated, 630 (40.6%) required medevac to a higher level of care. 283 were classified as "urgent," 151 "priority," and 184 "routine." Of these, 133 (21.5% of medevacs, 8.6% of all patients) required ERC. 130 (97.8%) of ERC patients were classified as "urgent," accounting for 45.9% of all "urgent" medevacs. ERC round-trip missions averaged 79.4±29.6 min (mean±SD) including 12.7±19.3 min on the ground at Echelon III for patient turnover. The sending medical unit provided all medical equipment/supplies required for transportation. Overall there were no adverse changes in vital signs or body temperature en route and no deaths during transportation. Only 25% of ERC missions were in Medevac (Army UH-60) helicopters, the majority being USMC CH46 troop helos (71%.) Primary reason for ERC was intubated status in 129 (97.0%) of ERC patients. 20 (15%) of ERC patients had chest tubes. Most common ERC interventions in flight were administration of IV sedation (80% of missions), paralytics (79%), narcotics (48%); continued transfusion (18%); ventilator changes (11%); and endotracheal tube manipulation (retaping or reinflating cuff, 6%.) No intubations, crichothyroidotomies, chest tube insertions/ manipulations or needle decompressions were performed en route, and only one new peripheral IV was inserted. Conclusions: (1) This first report of Navy En Route Care in OIF/OEF demonstrates that Navy nurses successfully transport critically injured patients without significant adverse events over brief mission durations. (2) ERC training should ensure that ERC nurses are familiar with ventilated patients and with equipment, medications, and airframes most likely to be encountered.

Determining the Effects of Multiple Mechanisms of Injury Due to Explosions on Casualty Outcome in the Shipboard Setting

Authors and Affiliations

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Research Priorities and Gaps: Numerous injury models have been developed by the military community to predict the probability of injury due to specific mechanisms of injury. Each model is being reviewed to identify its strengths and gaps. The effects of these combined mechanisms will determine injury, urgency of care, resources required and the effect on casualty outcome over time in the ONR funded Human Injury and Treatment (HIT) project.

Abstract

Injuries due to explosions are the result of multiple mechanisms of injury. Models have been developed by the military community over the past thirty years to predict probability of injury due to specific mechanisms. In order to predict the effects of these multi-mechanisms, injuries sustained by the crew and outcome of the casualty in a shipboard environment, new software must incorporate multiple modules. The Office of Naval Research has funded the Human Injury and Treatment (HIT) project to bring each of these separate modules together to develop a software tool which addresses these issues. Models for predicting injury due to blast overpressure, fragmentation, blunt trauma, burns, and the effects of toxic gas exposure were reviewed in detail for applicability to the shipboard setting. The models, mechanisms, and results of this review are listed in the table below.

INJURY MODEL	MECHANISM	RESULTS of REVIEW
INJURY	Blast overpressure to lung	Unvalidated conversion of data from sheep to humans
ORCA	Fragment penetration	Output in AIS 1985
BURNSIM	Burns	No location of burn or TBSA
TGAS	Toxic gas effects	Accounts for most common fire gases
Motor vehicle crash	Translocation and	No account for impacts due to large objects in motion or
injury criteria	Blunt impact	high coupling rates
Smoke inhalation	Fire	No model

The injury model outputs will be converted to injury descriptions using the Military Combat Injury Scale (MCIS) developed specifically for combat injuries. Although probability curves for risk of death for each mechanism of injury have been developed, the most difficult task will be to determine the cumulative risks of multiple mechanisms. A subject matter expert panel will assist the HIT team in determining the best approaches, which will then be tested using data from previous shipboard events and combat trauma registry data from Operations Iraqi and Enduring Freedom (OIF and OEF).

New Tools for Characterizing Shipboard Injury: Military Combat Injury Scale (MCIS) and Military Functional Incapacity Scale (MFIS)

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Research Priorities and Gaps: Despite revisions to the Abbreviated Injury Scale (AIS) resulting in a military version (AIS 2005-Military), multiple issues persist in using AIS coding to describe and assign severity to combat injuries. Thus, new tools were needed that would accurately characterize combat anatomic injury, and correlate immediate combat functional incapacity to severity of injury for shipboard and ground operations.

Abstract

A chronology of efforts, including development of a military version of the Abbreviated Injury Scale (AIS), AIS 2005-Military, failed to fully describe and assign severity to combat injuries. Thus, replacement tools were developed: the Military Combat Injury Scale (MCIS), which includes injury descriptors that accurately characterize combat anatomic injury, and the Military Functional Incapacity Scale (MFIS), which indicates immediate tactical functional impairment.

The following multi-step approach to developing the MCIS was used: (1) the AIS injury descriptors were reviewed for frequency of use, (2) injury descriptions were created to represent military-relevant body regions and severity, (3) injury descriptions were added to ensure that all current combat injuries are codable, and (4) immediate tactical functional incapacity was assigned to each injury severity level. Assignment of MCIS severity levels was based on increased risk of death or disability over time from each individual injury using a five-point scale ranging from minor to lethal. The MFIS was developed based on the casualty's ability to shoot, move, and communicate, and comprises four levels ranging from "Injured; able to continue mission" to "Injured; lost to military." Separate functional impairments were identified for injuries aboard ship which include impairments in vision, hearing, speech, dexterity, movement, strength/stamina and cognition. This allows the MFIS to be used for ground, vehicle-mounted, or shipboard forces.

The MCIS is a simpler, comprehensive severity scale that was developed specifically to characterize the unique injuries encountered in combat, especially those due to explosions. It correlates with the MFIS, which associates immediate combat functional impairment for minor and moderate severity injuries. In a shipboard environment, the MFIS score identifies casualties with essential skills who can contribute to the mission in an emergency situation and be treated when the tactical situation allows.

Predicting Individual Fatigue Resistance: Implications for Casualty Prevention through Optimized Crew Scheduling

Authors and Affiliations

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Research Priorities and Gaps: Casualty prevention.

Abstract

Background: Fatigue is a pervasive threat to Naval Aviation operations and personnel, compromising mission effectiveness while costing time, money, and lives. Current fatigue modeling tools, such as the Fatigue Avoidance Scheduling Tool (FAST), are group-based and assume an equal effect of fatigue across individuals. However, recent research suggests that large, stable individual differences in fatigue resistance exist. An understanding of individual differences in fatigue resistance should inform the development of more accurate, individually optimized predictive models, which could fundamentally improve scheduling and safety optimization to prevent mishaps. Purpose: To use baseline individual performance on basic cognitive tasks to predict fatigue resistance across time. Method: Fifteen active duty military personnel awaiting flight training at Naval Air Station Pensacola volunteered for the study. Participants completed a battery of neurocognitive and physiological assessments at rested baseline, and were subsequently re-tested every three hours over the course of 25 hours of continual wakefulness. Individuals' baseline performance was used to predict subsequent performance across time, thereby characterizing fatigue resistance. Results: Using Hierarchical Linear Modeling (HLM), baseline Psychomotor Vigilance Task (PVT) performance moderated the relationship between FAST predictions and PVT lapses across time (χ 2 [13] = 230.14, p < .001) in a manner consistent with individualized patterns of fatigue resistance. Discussion: These results are consistent with a growing body of empirical evidence that large, stable individual differences in fatigue resistance exist. Notably, the results show that these differences can be predicted at rested baseline using the PVT. Other researchers have found several cognitive tests of executive function to predict fatigue resistance. In light of these findings, the development of individualized predictive fatigue/performance models should be readily achievable. The ultimate incorporation of validated individualized fatigue prediction models into flight scheduling software is expected to improve mission effectiveness and prevent casualties through mishap reduction.

Tourniquets Exposed to the Afghanistan Combat Environment Have **Decreased Efficacy and Increased Breakage** Compared to Unexposed Tourniquets

Authors and Affiliations

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Abstract

We hypothesize that an anecdotally observed increase in tourniquet breakage and decrease in efficacy may be secondary to environmental exposure during military deployment. This was a clinical trial comparing efficacy and breakage of 166 Afghanistan-exposed tourniquets to 166 unexposed tourniquets. Afghanistan exposure was defined as tourniquet carriage by field staff in the operational environment for approximately six months. In the controlled environment of a US hospital, a previously exposed tourniquet was tested on one thigh of each subject, while an unexposed tourniquet was tested on the opposite thigh. We recorded tourniquet efficacy (absence of distal pedal pulse for at least 30 seconds), breakage, and the number of turns required to stop the distal pedal pulse. A Wilcoxon sign-rank test was used to test differences between exposed and unexposed tourniquets and logistic regression analysis was used to identify physical traits associated with efficacy and breakage. Tourniquets exposed to the environment broke more often (14/166 versus 0/166) and had decreased efficacy (63% versus 91%; p < 0.001). Three turns were required for most tourniquets to be efficacious. In multivariable analyses, tourniquet exposure was strongly associated with efficacy, and no subject characteristics, including body mass index and thigh circumference, were significantly associated with efficacy. Environmental exposure of military tourniquets is associated with decreased efficacy and increased breakage. In most cases, tourniquets require three turns to stop the distal lower extremity pulse.

A Promising Platform for Malaria Vaccines: Results from a Clinical Trial of a DNA Prime—Adenovector Boost Regimen to Prevent Plasmodium falciparum Malaria

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations. Casualty prevention.

Abstract

Background: Malaria causes approximately 243 million cases and 863,000 deaths annually and is one of the top infectious diseases that deployed personnel worldwide are vulnerable to. The most advanced malaria vaccine candidate, RTS,S, is a recombinant protein-based virus-like particle and confers 35-60% protection inducing mostly antibody-mediated and CD4+ T cell responses. Genetically based plasmid DNA and adenovirus-vectored vaccines induce strong CD8+ T cell responses, thus may offer an alternative mechanism of protection. Methods: This trial assessed the safety, immunogenicity, and efficacy of a prime-boost malaria vaccine in healthy, malaria-naïve adults. Three doses of a DNA vaccine consisting of two plasmids (Vical Inc.), encoding circumsporozoite protein (CSP, pre-erythrocytic stage antigen) and apical membrane antigen 1 (AMA1, antigen for both pre-erythrocytic and blood stages, 1 mg each), were delivered intramuscularly (IM) by jet injection (Biojector 2000®) at 4-week intervals. Sixteen weeks later, a boosting adenovectored vaccine (AdCA) was given IM by needle. The AdCA consisted of two serotype-5 adenovectors (GenVec, Inc.) encoding CSP and AMA1 (1×10^{10} pu each). Four weeks following AdCA boost, 15 immunized and six unimmunized subjects were challenged with P. falciparum sporozoites via five infected mosquito bites. Results: Both the DNA and AdCA vaccines were safe and well tolerated with no vaccine-related serious adverse events. All subjects developed parasitemia except four immunized subjects (26.7%) were sterilely protected 28 days post-challenge. Three of these had a strong cell-mediated ELISpot response to AMA1 or CSP + AMA1. Antibody response was poor (CSP) to moderate (AMA1). Conclusions: These exciting results demonstrate efficacy of a DNA-prime, adenovirus 5-boost vaccine regimen against falciparum malaria, the highest level seen with genetically based vaccines, and provide new insight into the mechanism of protection. Further clinical development will include adding additional malaria antigens or using adenovectors of other serotypes in order to improve protection.

A Processing Pipeline for in vivo Brain Magnetic Resonance **Spectroscopy for Diagnosing and Treating Neurotrauma**

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Research Priorities and Gaps: Post-traumatic stress disorder. Traumatic brain injury. Wound / injury management throughout the continuum of care.

Abstract

Understanding, diagnosing, and treating complex neurological conditions and disorders, such as traumatic brain injury (TBI), post-traumatic stress disorder (PTSD), and pain, has steadily gained attention in both military and civilian medicine. The fact that these conditions often co-occur in individuals compounds the difficulty in isolating the underlying etiology. However, advancements in a novel neuroimaging technique, magnetic resonance spectroscopy (MRS), provide promise for elucidating the nature of these complex disorders. In vivo brain MRS non-invasively collects a composite neurochemical spectrum from a specific brain voxel that can be quantitatively analyzed to diagnose neurotrauma.

Draper Laboratory has developed a novel suite of MRS biomarker discovery and classification algorithms (BIDASCA) to analyze in vivo brain MR spectroscopy data. The pipeline begins with post-acquisitional processing algorithms to mitigate distortions arising from a variety of sources (e.g., macromolecules, water, scanner). Subsequently, feature extraction and statistical testing algorithms identify discriminating biomarkers that highlight meaningful differences between healthy and diseased states and can subsequently be used by classification and validation algorithms to enable reliable classification of unlabelled MRS signals.

A recent publication involving the current authors [Stanwell et. al] contrasted the spectral content of voxels from control subjects with those who suffered from spinal cord injury (SCI). The pipeline is being augmented for new studies involving TBI and PTSD, as well as chronic traumatic encephalopathy (CTE) incurred during sports injuries.

We believe this effort provides the foundation for diagnosis in both acute and chronic disease states as well as evaluating the efficacy of a therapeutic regimen. Quantitative analysis of imaging technologies, such as demonstrated using BIDASCA for MRS, provides an entry point for fusing heterogeneous data into a broader, multi-modal framework for understanding complex neurological disorders.

Nanotechnologies and Hemostatic agents

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Research Priorities and Gaps: Wound management. Mitigation and treatment of neurotrauma. Rapid blood treatment.

Abstract

As much as 50% of surgical time can be spent packing wounds to reduce or control bleeding. Therefore, hemostatic devices that are able to decrease bleeding, reduce operative time, and improve the quality of surgical tissue management are becoming increasingly essential components of the surgeon's toolbox. According to the literature, the five most important performance characteristics of the ideal hemostat are safety, efficacy, usability, cost, and approvability. Now, as nanotechnology is rapidly ushering in new medical technologies, there is a new class of hemostatic agent that stops bleeding in less than 15 seconds in multiple tissues as well as a variety of different wounds, with the potential to radically reduce the quantity of blood needed during surgery in the future. This is the first time that nanotechnology has been applied in a surgical setting for animal models to stop bleeding and NHS-1 seems to demonstrate a new class of hemostatic agents that does not rely on heat, pressure, platelet activation, adhesion, vasoconstriction, or desiccation to stop bleeding.

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Bringing Novel Clinical Advances from the Bench to the Bedside: Translational Medicine at the Naval Health Research Centre

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations. Advanced forward care. Casualty prevention.

Abstract

Whether in response to the recent pH1N1 influenza pandemic or the emergence of antibiotic resistance bacteria that carry the New Delhi metallo-beta-lactamase (NDM-1) enzyme, public health officials and military planners must reconsider conventional medical responses against 21st century pathogen threats. Translational Medicine (TM) approaches augment the prediction, prevention, diagnoses and treatment of infectious diseases. In work supported by the Armed Forces Health Surveillance Center, the Naval Health Research Center (NHRC) conducts in-depth population-based surveillance of infectious pathogens in operational environments, contributing a wealth of data to ascertain disease risk and providing a valuable collection of well-characterized biological samples to address the safety and efficacy of new diagnostics and therapeutics. Since 1996, the Respiratory Disease Department at NHRC, utilizing cutting-edge technology, has developed a portfolio of basic and applied biomedical research projects and clinical trials through partnerships with industry, government and academic collaborators. This work resulted in the first and only FDA-approved point-of-care diagnostic for H5N1 Avian Influenza (Arbor Vita corporation) and, in April 2009, the identification of the first pandemic influenza case on the US-Mexico border utilizing the DARPA-funded IBIS T-5000 platform. NHRC conducted Phase III testing of Duramed Pharmaceutical's adenovirus vaccine and are currently embarked on trials to measure adverse events associated with smallpox vaccination in deploying military personnel and work to assess protective immune responses against Japanese encephalitis Virus (JEV) in Marines vaccinated with the new IXIARO JEV vaccine. In response to emerging drug resistance in circulating influenza viruses, NHRC has partnered with Adamas Pharmaceuticals and the National Institute of Allergy and Infectious Diseases to test Triple Combination Antiviral Drug therapy in at-risk influenza patients, taking advantage of already FDA-approved drugs. NHRC uses cutting edge technologies to advance novel diagnostics, vaccines, and therapies from the bench to the bedside of ill warfighters and their families.

Effects of Hyperbaric Hyperoxic Stress on Expired Nitric Oxide and Expired Carbon Monoxide in Divers

Authors and Affiliations

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Research Priorities and Gaps: Undersea medicine—diving and submarines. Wound / injury management throughout the continuum of care.

Abstract

The US Navy currently conducts hyperbaric oxygen (HBO) treatments for a variety of medical conditions including decompression treatment, carbon monoxide poisoning, wound healing, and crush injuries for which pulmonary O₂ toxicity is a potential side effect. HBO treatment is also being investigated as a treatment for traumatic brain injury. Furthermore, Special Operation divers who use closed circuit underwater breathing apparatus (i.e. LAR-V and MK-16) that operate at high O₂ partial pressures are mission limited by lung problems caused by high oxygen levels. Understanding the primary mechanisms responsible for individual susceptibility to hyperbaric oxidative stress would allow us to tailor HBO therapy according to the specific needs of the patient leading to more efficient and less toxic HBO treatment profiles. Furthermore, an improved understanding of pulmonary oxygen stress that leads to even small increases in acceptable PO₂ exposures could potentially translate into more efficient decompression procedures for military divers, as well as greater mission capability for Special Operations Forces divers (i.e. longer/more frequent dives).

Recently, exhaled nitric oxide (NOexp) and carbon monoxide (COexp) have been studied as markers of airway inflammation/oxidative stress in a variety of lung diseases, but the importance of these exhaled gasses as a marker of the oxidative stress response of the lungs to HBO is unclear. At NSMRL we are currently conducting studies designed to determine 1) if NOexp and/or COexp can serve as noninvasive physiological markers of hyperbaric oxidative stress in humans and 2) the influence of HBO dosage on biochemical factors associated with nitric oxide production in the lungs and systemic circulation. This presentation will focus on data collected on divers exposed to 2 ATA of HBO for between one and eight hours and will show how the post-dive changes and recovery in NOexp and COexp are affected by the dosage of the hyperoxic hyperbaric exposures.

Funded by the Office of Naval research (work unit #N0001410WX30014) through the In-house Laboratory Independent Research (ILIR) program and the Defence Health Medical Research and Development Program.

Submariner Health: Experimental Evaluation of Exposure Limits for **Key Inhaled Compounds**

Authors and Affiliations

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Research Priorities and Gaps: Undersea medicine—diving and submarines.

Abstract

Background: Typical atmospheres aboard US Navy submarines include increased carbon dioxide (CO₂) and increased carbon monoxide (CO), with low levels of oxygen (O₂). Existing exposure limits for these compounds were developed based on male effects only and do not currently take into account potential effects on female crew member reproduction and the development of offspring. Experiments need to be conducted to fill these data gaps. Objective: To determine if current exposure standards for these three key chemicals found in submarine atmospheres are protective of all crew members, male and female. Methods: NAMRU-D has designed a multiphase study to evaluate safe exposure limits for CO₂, CO and O₂. Phase 1 of the study will evaluate toxic effects in rats from 23 hr/day exposures to three different mixtures of these compounds. Endpoints to be evaluated include: survivability, estrous cycles (female), hormonal profiles, and histopathology of key organ systems. In addition to the endpoints examined during Phase 1, Phase 2 will evaluate the reproductive success of the exposed rats, as well as give initial information on developmental effects that might be seen in the offspring of parents exposed for longer periods. Phase 3 will be a modified 2-generation reproductive/developmental study in which the parents are exposed for 90 days. Impact: A key aspect of the Navy Surgeon General's research priorities is the protection of submariner health. The results from this study will directly support this priority by providing data relevant to re-evaluating the existing exposure limits for CO₂ CO, and O₂. Additionally, the protocols developed and refined during this work will serve as a "benchmark" to be used for testing other atmospheric chemicals present aboard submarines for which appropriate toxicity data are also not yet available.

Neurotechnological Approaches to Trauma Spectrum Disorder: Implications and Obligations for Navy Medicine

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Research Priorities and Gaps: Traumatic brain injury and PTSD research, prevention and treatment.

Abstract

Background: Current wars in Iraq (Operation Iraqi Freedom, OIF) and Afghanistan (Operation Enduring Freedom, OEF) have returned thousands of troops with trauma that incur durable biological, psychological, and social consequences. Of particular note are those neuro-psychiatric sequelae that incur a range of cognitive, emotional, somatic, and behavioral effects—including anxiety, depression, pain, substance use and social disruption. We propose that these effects represent a neuro-psychiatric spectrum disorder that involves genetic predispositions and environmentally-dependent expressions of certain neuro-cognitive phenotypes. Our ongoing work supports the potential for the development and progression of certain types of neuro-psychiatric pathology resulting from a variety of environmental insults and/or trauma that leads to the over-production of neuro-inflammatory mediators, results in altered neural and glial function, and produces an often latent central neuroinflammatory syndrome—inclusive of neurological, psychological and somatic signs and symptoms. 1-4 Ultimately, this produces a constellation of recurrent psychological features (e.g. anxiety, agitation, depression), neuro-behavioral effects (e.g. attempts at self-medication through escalating substance use including alcohol and prescription/nonprescription/illicit drugs^{1,4,6}), somatic features (e.g. occurrence and/or exacerbation of chronic pain, initiation or intensification of autoimmune disorders, and alterations in appetite, sleep, energy/executive function, and libido¹⁻³), and social manifestations (e.g. relational discord, vocational disruption^{1-4,6}). Objective: We opine that this is a form of trauma spectrum disorder (TSD), and that that identifying substrates and mechanisms of TSD will be of vital importance to the development and use of new techniques and technologies that can be used in concert with extant approaches to assess, prevent and/or mitigate the debilitating bio-psychosocial manifestations of such pathology. Methods: This is a novel conceptualization of these pathologies, and our work is dedicated to employing systematic analysis to more thoroughly elucidate this concept and identify and analyze current gaps in information and the use of science and technology in prevention, assessment and treatment of TSD, and proposing methods for de-limiting extant gaps in the use and viability of such techniques and technologies in both research and clinical practices. Results: To date, our studies have revealed the viability, and under-use of, neurogenetic, neuroimaging, neurobiomarker and neuro-cognitive approaches in the identification,

assessment (and possible prevention/mitigation) of TSD. This establishes opportunities for improved definition, prevention, diagnosis and treatment of such disorders that we opine are obligatory as an ethical maxim of military medicine. **Impact:** We believe that the use of such cutting edge approaches are of particularly current importance given (a) the persistent disconnect between state-of-the-art research and its translation into the most effective clinical practices,⁵ (b) the continued incidence and prevalence of these disorders in the military population, and (c) the impending shift in categorization of these disorders – and the quality of their care – as a result of the forthcoming release of fifth edition of the American Psychiatric Association's *Diagnostic and Statistical Manual (DSM-5)* in 2013.⁶

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Interactive, Rich-Media, Self-Documenting System on Handheld Devices for Medical Procedures and Decision Support

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Research Priorities and Gaps: Undersea medicine—diving and submarines. Medical systems support for maritime and expeditionary operations. Advanced forward care.

Abstract

In submarines, forward care, and other remote contexts, IDCs, medics, and similar personnel who are not trained physicians are very frequently responsible for providing medical care and helping to make decisions about evacuations of ill or injured crewmembers. Medical decisions they make can have serious consequences on the health of the crewmember and severely impact mission objectives and security of the vessel. The burden and stress on the submarine medic can greatly increase when the crewmember is female. The award-winning guideVue system for mobile health and mobile learning enables complex medical diagnostic/treatment procedures to be presented on Windows and on mobile platforms, including iPads, iPods, Android tablets and others in an intuitive, structured, and guided step-by-step format accompanied by rich media, i.e., text, audio/voice, images, and video/animations. The system can operate without network connectivity and provides automated documentation of care. Every step of the clinical guideline followed for a particular encounter is tracked and saved into a time/location-stamped, encrypted treatment log. This is imported into the guideVue Data Manager, a SQL-compatible database implemented in Microsoft Access, thus enabling production of detailed case histories, statistical analysis, and reports. An Authoring tool enables creating or editing of these 'guideVues' with a simple point-andclick interface without programming. In addition to point-of-care decision support, the guideVue system also enables mobile learning of any topic together with student performance assessment.

The system has received support from the US Army Telemedicine Advanced Technology Research Center. A project is underway to convert selected sections of the Special Operations Forces Medical Handbook to the guideVue system. A recent study, supported by a competitive grant from Microsoft Research, among health care workers (not physicians or nurses) showed statistically significant 35% error reduction, 33% increase in protocol compliance, and decrease in mental workload and frustration while displaying very high acceptance and usability. In this talk we shall describe the system with live demonstrations, present results from a prospective, randomized, controlled study, and discuss its potential to improve medical care in submarine, forward care, and as support for maritime and expeditionary operations.

Comparison of Mechanical Work during Walking between Military Patients with Traditional and Ertl Transtibial Amputations

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Research Priorities and Gaps: Prosthetics—functional outcomes. Condition directly relevant to injuries on the battlefield. Warfighter restoration.

Abstract

This study examined kinematic and kinetic measurements taken in the Biomechanics Laboratory at NMCSD to evaluate the functional outcome of rehabilitation of patients with two types of transtibial amputations. These data and the mechanical work required to walk were evaluated for transtibial amputees who underwent either a Traditional or Ertl amputation and have been ambulating without an assistive device for at least twelve months. Thirteen patients met these inclusion criteria, seven having undergone the Ertl procedure and six the Traditional amputation. Ertl and Traditional patients had similar height and weight. Table 1 lists the descriptive statistics of the two groups while kinetic and kinematic data are included in Table 2 and Table 3 respectively. Statistical analysis did not show a significant difference for any of the spatiotemporal parameters between the two groups at self-selected and fast speeds, but did find a significant discrepancy when evaluating residual limb length and the ground reaction force produced in late stance (F3) by the prosthetic leg (PL). The Ertl patients had a longer residual limb length. Calculations of mechanical work revealed that Ertl patients use 1147.4 ± 226.5 Joules (J)/stride on their PL and 1145.7 ± 228.7 J/stride on their NonPL. The mechanical work values for the Traditional patients were 1201.3 ± 316.6 J/stride on the PL and 1204.4 ± 322.4 J/stride on the NPL.

These data do not show any functional kinematic, kinetic or differences in mechanical work during walking that would make one technique more favorable to the other. Indications are that the patients with the Ertl procedure are no more efficient ambulators than patients with a Traditional approach. Due to the longer operative time and longer post-operative non-weight bearing period associated with the Ertl procedure, the Traditional approach to transtibial amputations may be favorable in this active population.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

Preparing for the Stress of Combat: THE DOCS Graphic Novel and Video Animation

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Research Priorities and Gaps: Post traumatic stress disorder. Traumatic brain injury.

Abstract

Many military personnel with combat stress-related concerns are reluctant to seek care due to personal embarrassment, belief that their peers and leaders would lose confidence in them, and a variety of other factors. To help combat veterans "reset" to more adaptive ways of thinking and behaving during and following deployments, and to reduce mental health stigma and encourage appropriate help-seeking, the Naval Health Research Center has developed a variety of educational messages and tools in diverse formats. These resources are complementary with Navy Medicine's efforts to improve psychological health outreach

Specifically, in-theater behavioral health surveillance indicates that expeditionary Corpsmen experience high levels of psychological strain, stemming from their exposure to direct combat as well the significant demands they experience as medical professionals called upon during life-threatening medical emergencies. To help familiarize Corpsmen with the stresses of combat deployment, and to encourage discussion of the wear-and-tear experienced by providers in the warzone, NHRC has developed a graphic novel titled "THE DOCS" that follows four Corpsmen through a deployment in Iraq and illustrates the struggle to readjust upon returning home. In addition to the print version, the graphic novel was adapted to video animation, which can be viewed on devices such as IPods or MP3 players. Both the graphic novel and the video will be highlighted during this presentation.

Identifying Biomarkers that Distinguish Post Traumatic Stress Disorder and Traumatic Brain Injury Using Advanced Magnetic Resonance Spectroscopy

Authors and Affiliations

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Research Priorities and Gaps: Post traumatic stress disorder. Traumatic brain injury. Wound/injury management throughout the continuum of care.

Abstract

Mild traumatic brain injuries (mTBI) and post traumatic stress disorder (PTSD) are estimated to be among the most common injuries sustained by U.S. military forces deployed in service of Operation Iraqi Freedom and Operation Enduring Freedom. However, symptoms associated with PTSD and mTBI frequently overlap and can be both subtle and transient. There is currently no objective way of definitively diagnosing each of these injuries other than questionnaires or self diagnosis by the soldier. Our research addresses these critical gaps in the diagnosis of American soldiers by using an emerging, non-invasive neuroimaging technology, MR spectroscopy (MRS). MRS can accurately diagnose neurological disorders such as brain tumors, Alzheimer's disease, and chronic pain. These studies have shown that MRS chemical changes precede changes recorded by current imaging modalities and therefore has potential to provide an objective tool for the diagnosis and treatment monitoring of PTSD and mTBI.

Using advanced MRS methods and biomarkers discovery and classification algorithms, our objectives are to: (1) enable earlier detection and disambiguation of mTBI and PTSD based on objective measures from changes in brain biochemistry, (2) provide the foundation for return-to-duty decision making based on the tracking of specific MRS biomarkers, and (3) contribute uniquely to the understanding of the pathophysiology for mTBI and PTSD that other modalities are unable to provide.

The purpose of this presentation is to describe the technological advancements that will allow us to achieve the described aims and our progress to date to achieve these aims. This will include an explanation of one-dimensional and two-dimensional spectroscopy and the brain chemicals, or metabolites, and their roles in mTBI and PTSD.

Restoration of Internal Models of Grasp in Users of Myoelectric Prosthetic Hands

Authors and Affiliations

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Research Priorities and Gaps: Prosthetics. Warfighter restoration.

Abstract

The goal is to develop methods to improve the performance of myoelectric prosthetic hands. Recent technological advancements in the capabilities of upper extremity prosthetics promise to someday allow warfighters to return to active duty without limitations in physical performance. Optimizing prosthetic performance may rely on training users to employ control strategies used by uninjured subjects. Motor control studies of human grasp have shown that the CNS relies on internal models to efficiently manipulate objects. These models include aspects of the object (weight, friction, center of mass) as well as aspects of the end effector (relationship between muscle activation level and grip force). A simple griplift task has been used in subjects with stroke and peripheral nerve injuries to study the fidelity of these internal models after injury. This task involves squeezing two vertical sides of an object, lifting it off a surface and holding it steady. Internal models are used to generate a feed-forward motor plan for coordinating the grip and lifting forces on the very first trial. Characteristics of normal behavior are coordinated increases in grip and lift force, grip and lift force rates that increase with object weight, plateau of forces at lift off, and rapid adaptation to novel objects within a few trials. Data from a single highly experienced user showed use of an internal model during task performance; the grip force during the holding phase correlated with object weight and lift force rates increased with higher weights. However the subject re-gripped on several occasions during lifts, indicating errors in the internal model. These errors may be due to lost tactile sensation, which is important for model development and maintenance. This suggests that methods might be developed to retrain internal models using feedback approaches that substitute for lost tactile sensation during task practice.

Domestic Violence Screening of Obstetric Triage Patients In a Military Population

Authors and Affiliations

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations.

Abstract

Objective: Domestic violence has been shown to be increased in emergency care settings and may also be increased in pregnancy and military populations. The purpose of this study was to estimate the selfreported prevalence of domestic violence in a pregnant military population presenting for emergency care and to determine the acceptability of domestic violence screening in these patients. Methods: This was a prospective observational study of patients presenting for obstetric emergency care to Naval Medical Center Portsmouth, a large tertiary care military treatment facility in Portsmouth, VA from October 2008 to June 2009. Participants were anonymously screened for domestic violence using the Abuse Assessment Screen. Chi-square univariable analysis identified variables that had crude associations with abuse. Mann-Whitney tests were used for ordinal data. Mulitvariable logistic regression provided adjusted odds ratios and confidence intervals. Results: Of the 461 surveys collected, 104 (22.6%) of respondents screened positive for abuse (either current abuse or a prior history of abuse). Physical abuse in the past year was reported by 19 women (4.1%), with the majority reporting abuse by current husband or boyfriend. Thirteen women (2.8%) reported abuse since becoming pregnant, with the majority reporting abuse by husband or boyfriend. Conclusions: The self-reported prevalence of domestic violence in a pregnant military population presenting for emergency care was 22.6%. The majority of women surveyed were not offended by abuse screening and also felt that patients should be routinely screened for abuse.

Does Testing Positive for Gonorrhea or Chlamydia in the First Trimester of Pregnancy Affect Fetal Outcomes?

Authors and Affiliations

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Research Priorities and Gaps: Human injury and treatment model. Crew medical assessment.

Abstract

Study Objective: The purpose of this study was to compare fetal outcomes of first trimester pregnant women found to have a positive test for Neisseria gonorrhae or Chlamydia trachomatis (GC/CT) versus those who were negative following emergency department (ED) presentation for abdominal pain or vaginal bleeding. Methods: A retrospective chart review of consecutive ED records from December 2005 to August 2006 was performed to identify pregnant women presenting for evaluation of vaginal bleeding or abdomino-pelvic in their first trimester (estimated gestation age ≤12 weeks by last menstrual period) who were also tested for GC/CT during their visit. Standard GC/CT unisex endocervical swab was used for testing. We excluded patients with multiple presentations during the same pregnancy. Demographic data, results of GC/CT testing and fetal outcomes were documented. Results: A total of 1144 first trimester women presented for evaluation in the ED. 651 met inclusion criteria with 85 (13%) lost to follow up. The final group had 566 patients, 29 of whom tested positive for GC or CT (5.1%). 17 of these women delivered (58.6%; 95% CI 40.7–76.6%) and 12 had a spontaneous abortion (SAB) (41.4%; 95% CI 23.5–59.3%). None of the 29 patients with a positive GC/CT test had an ectopic pregnancy. Of those with a negative GC/CT test, 340 delivered to term (63.5%; 95% CI 59.2-67.4%), 23 had an ectopic pregnancy (4.5%; 95% CI 28.4-36.4%), and 174 experienced a SAB (32%; 95% CI 28.4-36.4%). In a subgroup analysis, 379 women had a live intrauterine pregnancy documented during the ED visit. 361 women had a negative GC/CT test with 67 experienced a SAB (18.6%; 95% CI 14.5-22.6%). 18 women had a positive test for GC or CT and also a live IUP with only 4 experiencing a SAB (22.2%; 95% CI 3.0–41.4%). Conclusion: In this small study, the GC/CT incidence was 5.1%. Spontaneous abortion occurred in 41.4% of women who tested positive for GC/CT in the first trimester. This was compared to an overall fetal loss of 36.5% of women with a negative test. GC/CT infections did increase the rate of fetal loss by an odds ratio of 1.22; however, these results were not statistically significant.

Using Vigabatrin for Reducing the Incidence of CNS Oxygen Toxicity Associated with Oxygen Pre-breathe at 132 FSW

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Research Priorities and Gaps: Mitigation and treatment of neurotrauma. Casualty prevention.

Abstract

Background: Oxygen is the most widely used therapeutic strategy to prevent and treat DCS. Oxygen prebreathe at 60 fsw virtually eliminates DCS in swine saturated with nitrogen and rapidly decompressed. The Navy Therapeutic Treatment Table 6 is predicated on the use of oxygen as an adjunct to recompression therapy. Oxygen therapy at depth has its risks; as the partial pressure of oxygen increases, so do its toxicity. CNS oxygen toxicity is the most severe side effect hyperbaric oxygen (HBO); the most serious manifestation is seizure. To extend oxygen prebreathe strategies to 132 fsw an adjunctive therapeutic must be administered to control/prevent seizure onset. The FDA approved antiepileptic Vigabatrin has been effective in preventing HBO-induced seizures in rats to 132 fsw. Objectives: A single 180 mg/kg dose of Vigabatrin eliminates HBO-induced seizure at 132 fsw in rats. Furthermore, a single 250 mg/kg dose 24 hours prior completely eliminates oxygen-induced seizure at 5 ATA indicating long-lasting efficacy. The primary objective is to decrease HBO seizure in the 20 kg swine model developed at NMRC at 165 fsw using Vigabatrin at both the human recommended dose and the lowest efficacious dose in rat studies. The secondary objective is to determine whether visual field constriction, the primary side effect of chronic Vigabatrin use, occurs following acute administration. Methods: 30 male swine 20-25kg prepared for diving, including EEG electrode placement and pre-dive electroretinograms (ERGs). Thirty minutes prior to dive animals will be randomized to receive i.v. Vigabatrin (50mg/kg; or 180 mg/kg) or Saline. Animals will then be pressurized on air to 132 fsw. On bottom the breathing circuit will be switched to 100% O2. Seizure onset monitored by EEG, which will be confirmed visually. Animals will be surfaced following seizure onset or 3 hour bottom time. Upon surfacing a post-dive ERG will be conducted and compared to the pre-dive ERG to assess for visual field defects. **Results:** Dives (n=30) to 165 fsw using oxygen resulted in seizure onset <8 min in control animals. Vigabatrin (180mg/kg) significantly increased seizure latency to 15 min.

Post-Concussion Syndrome, Post Traumatic Stress Disorder and Chronic Traumatic Encephalopathy: Common Genesis and Treatment Options

Authors and Affiliations

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Abstract

PCS, PTSD, and CTE are devastating neurological conditions not completely understood in terms of their pathogenesis. There is however, accumulating scientific evidence that physical injury, as in football or other contact sports as well as some psychiatric disorders (e.g. depression and PTSD), produce a neuro-inflammatory response in the brain. In the case of concussions, cumulative injury may lead to progressive neuro-degeneration of the brain (CTE). One of the authors (RB) named this neuro-inflammatory process "immunoexcitotoxicity," which he first observed in the "Gulf war syndrome." This process relates to an over-reaction of the resident macrophage immune protective cells in the brain (microglia). When stimulated by trauma, viruses or other toxic substances, they normally release chemicals (cytokines) that initiate a cascade of effects that, if failing to "switch off", further leads to a series of molecular chain reactions called "excitotoxicity." This can result in the eventual death of nerve cells. It is akin to a smoldering brush fire (inflammation) in the brain that with repeated trauma burns out of control. This process also occurs in other neurological diseases like Alzheimer's disease, multiple sclerosis, and Parkinson's

Immunoexcitotoxicity represents a new concept in medicine in the development of brain diseases and can explain the original observations of subsequent progressive brain injury (pugilistic dementia) in fighters, in other contact sports and in injury suffered in military combat. This immunoexcitotoxic response may be enhanced by prior "priming" of the microglia by exposure to neurotoxic metals (Pb, Al, Hg, Cd, Fe), neurotoxic chemicals, (pesticides/herbicides), prior or occult infections, and brain trauma (concussions). With subsequent concussions, as in a previously primed immune allergic reaction (e.g. peanuts), there is an outpouring of cytotoxic chemicals that is associated with memory loss, personality changes, depression and more--all common findings in PCS, PTSD, and CTE. Elevated levels of the same immunoexcitotoxic chemicals (IL-1, IL-6, TNF) seen in brain trauma have now been observed in depression, obsessive compulsive disorder, and other psychiatric disorders—unrelated to physical trauma to the brain. Thus, there appears to be a continuum from traumatic concussion to post-traumatic stress disorder to chronic traumatic encephalopathy—all with the underlying substrate of immunoexcitotoxicity. With neuroinflammation as a possible common genesis to all, preventive and therapeutic strategies with antiinflammatory agents both pharmacologic (NSAIDS, tetracycline's, etc.) and natural (Omega 3 fatty acids, vitamin D3, resveratrol, curcumin, quercetin, magnesium, luteolin, and hyperbaric O2, etc.) should be thoroughly investigated.

An fMRI Study of TBI Associated with Blast Injury

Authors and Affiliations

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Research Priorities and Gaps: Traumatic brain injury.

Abstract

Blast related traumatic brain injury (TBI) is sparsely documented in the present medical research literature. Given the complex patterns of axonal injury believed to underlie blast-specific injury, a reliance on conventional neuroimaging techniques may be partly responsible for this deficiency. Novel brain imaging techniques provide promise for increasing neuroimaging sensitivity in this patient population. Specifically, functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) represent opportunities for enhancing utility of imaging in the study of blast related TBI, potentially leading to improvement in rehabilitation therapies. Using these imaging modalities, we are conducting a dual cohort study to characterize the pattern of brain activation during performance of cognitive control and working memory tasks in service personnel with mild and severe TBI imaged between 3 and 42 months post injury. Among the primary goals of this study are to investigate the correspondence between: cognitive reserve, executive function, neuropsychiatric co-morbidity, overall outcome and, performance on cognitive control and working memory tasks with fMRI BOLD activation in patients with blast associated TBI. Following anecdotal reports from military neurologists on a characteristic and pronounced deficit in word retrieval ability among blast-exposed TBI patient population, a final goal of the study is to investigate the relationship between performance on a confrontational naming task and fMRI BOLD activation within these patients. To date, 447 patients with TBI at Walter Reed Army Medical Center (WRAMC) have been screened. Thirteen patients diagnosed with TBI, resulting from blast, have met eligibility criteria and enrolled in the protocol. Nine patients have completed the neuropsychological testing and four have completed subsequent MRI series. National Naval Medical Center (NNMC) has been added as a research site to address the unexpectedly low rate of eligible patients at WRAMC and consequent slow recruitment into the protocol.

Impulse Noise Hearing Loss Prevention Using N-acetylcysteine

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Research Priorities and Gaps: Hearing protection and restoration.

Abstract

Objective: To determine whether noise-induced hearing loss may be prevented with military occupational exposures if the antioxidant N-acetylcysteine (NAC) is administered along with the use of standard hearing protection devices. Study Design: Prospective, randomized, double-blind study. Setting: Marine Corps Recruit Depot (MCRD), San Diego, CA. Subjects and Methods: Healthy volunteers subjected to military noise during a 16-day period at the end of a mandatory four-week weapons training evolution. All subjects were issued standard Hearing Protection Devices. 612 subjects were randomized to receive either placebo (n=313) or treatment (n=299) with NAC two grams BID for 16 days. Conventional frequency pure tone audiometry, high frequency audiometry, tympanometry were assessed for each subject at baseline and post-treatment to establish presence or absence of hearing threshold shifts. Comparisons to elicit the effects of concurrent NSAID use and smoking history on significant threshold shifts were also obtained. Results: There was no significant difference in the percentage of significant threshold shifts (STS) between NAC and Placebo with either ear STS of 41.8% vs. 37.7%. Threshold shifts were examined in left, right, either and both ears, with p values ranged from 0.36-0.87 for STS. Conclusions: Threshold shifts were present in both groups. NAC at 2 grams twice daily as administered in this study was not effective in reducing the rate of STS or change in baseline of individual frequencies.

Evaluation of Intestinal Viability Using 3-CCD (Charge Coupled Device) in Children Undergoing Appendectomy

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Research Priorities and Gaps: Human injury and treatment model. Crew medical assessment. Automated critical care systems (ACCS).

Abstract

Introduction: The surgeon's ability to determine intestinal viability is limited to subjective measures of visual clues of perfusion. This inability to accurately determine viability presents a conundrum for the surgeon. In our laboratory, we use 3-CCD technology to separate visible light into its three primary wavelengths; by using an easily implemented mathematical algorithm, the amount of light detected by the CCDs can be directly correlated with tissue oxygenation. In this study, we report the use of 3-CCD technology to determine intestinal perfusion by using an appendectomy model for ischemia. **Methods:** In this study, we sequentially recorded 10 laparoscopic appendectomies for appendicitis. In brief, the recorded images are analyzed by selecting three regions of interest (ROIs) and evaluating the intensity levels (a.u.) at various locations along the appendix. Figure 1A demonstrates the enhanced image of an ischemic appendix during an appendectomy. The black box indicates the fat ROI, the white boxes indicate the appendix ROIs, and the dashed black boxes indicate the colon ROIs. The colon was used as a control for normal perfusion and a ratio to fat was performed to normalize the data. Results: As an indication of decreased perfusion, the appendix demonstrated a significant reduction in mean ROI values over time. Fat normalized ROI intensity values calculated for the colon, appendix, and distal appendix were $R^2 = 0.02$, $R^2 = 0.92$, and $R^2 = 0.89$ respectively. **Conclusions:** In this cardinal study, we have demonstrated proof of principle for 3-CCD technology to determine bowel ischemia. We have conclusively demonstrated reduced intensity levels in areas of known ischemia. Given the ability of this technology to identify areas of ischemia, this technique has the potential to significantly change the management of malrotation with volvulus, necrotizing enterocolitis and intestinal reconstruction in the future

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Effects of Tympanomeatal Blunting on Sound Transfer Function

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Research Priorities and Gaps: Wound / injury management throughout the continuum of care. Other conditions directly relevant to injuries on the battlefield. Hearing protection and restoration.

Abstract

Objective: (1) Measure the peak to peak displacement of the round window membrane (RWM) prior to blunting procedure. (2) Evaluate the impact of blunting the anterior tympanomeatal angle (ATA) on middle ear sound transfer function. Study Design: basic science study. Setting: Cadaveric temporal bone research laboratory. Subjects and Methods: Six fresh human temporal bones were prepared using a mastoidectomy and facial recess approach. Baseline RWM peak to peak displacements were obtained by single point laser Doppler Vibrometry (LDV) at 90 dB SPL over a spectrum of 250 – 8,000 Hz. Temporalis muscle was harvested and then fashioned into a graft for each temporal bone mimicking ATA blunting. RWM displacement responses with the blunted ATA were measured using the LDV to judge the impact on middle ear transfer function. Results: For each of the six temporal bones, the average displacement decreased across all sound frequencies with the ATA blunting when compared to baseline (no blunting). Baseline velocity measurements for all sound signals averaged $4.5 \times 10^{-3} \pm 1.892 \times 10^{-3}$ (mean \pm SEM) mm/sec while measurements averaged $2.2 \pm 6.62 \times 10^{-4}$ mm/sec with blunting of the ATA. (P<0.001) This amounted to a 52% decrease in velocity of the RWM following blunting of the ATA. Conclusion: Blunting of the ATA decreases the sound transfer function of the tympanic membrane and middle ear. Prevention of blunting at the ATA during tympanoplasty should be emphasized.

Altered Parietal Cortex Activations in Response to Emotional Pictures in Subjects with PTSD and TBI

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Research Priorities and Gaps: Post traumatic stress disorder. Traumatic brain injury. Wound / injury management throughout the continuum of care.

Abstract

Military combat in the current wars in Afghanistan and Iraq often expose warfighters to blast-related traumatic brain injury (TBI) that can result in structural brain injury as well as psychological trauma such as posttraumatic stress disorder (PTSD). Very little is known about systematic changes in electroencephalographic (EEG) activity with TBI, PTSD or the combination of the two. Subjects were male U.S. military veterans who served in combat situations during their tour of duty. Two thirds of the subjects experienced traumatic brain injury (TBI) primarily due to blast exposure during their deployment. Half of these subjects also developed PTSD symptoms as a result of their military service. The last third of the subjects had neither TBI nor PTSD. EEG data were collected from 136 scalp and face electrodes during performance of picture viewing and rating to assess emotional processing in the brain. EEG data were decomposed using independent component analysis (ICA) to isolate independent sources of EEG activity. Independent components (ICs) were clustered across subjects, based on location of bestfit equivalent dipoles, scalp map, and mean power spectral similarities. Subjects with both PTSD and TBI showed an enhanced late positivity (~300 ms) in parietal ICs following onset of emotional pictures. In particular, the late positivity was much larger than the early positivity ~125 ms, a feature that was not observed in TBI-only or control subjects. The results suggest altered early emotional processing in subjects with PTSD that might serve as a basis for electrophysiological diagnosis of PTSD and differentiate it from other disorders.

The Potential Effect of Jet Fuel Exposure on Noise Induced Hearing Loss

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Research Priorities and Gaps: Hearing Protection and Restoration.

Abstract

Background: Noise-induced hearing loss (NIHL) is a major military operational health hazard. Although widespread hearing conservation measures have been adopted, NIHL is as high as 20-30% in the military. Noise exposure standards have historically been based on the range of human auditory sensitivity and exposure duration; however recent research has established that simultaneous and even successive exposure to noise and specific chemical agents can potentiate NIHL or produce additive effects. Objective: To determine the extent of hearing loss from exposures to both noise and jet fuel. Methods: Rats were exposed for 6 hr/day, 5 days/week for 4 weeks to noise (Study 1: 0, 75, 85, and 95dB), noise and JP-8 (Study 2: 85dB, at concentrations of 200, 750, and 1500 mg/m3), JP-8 (Study 3: 200, 750, and 1500 mg/m3), and a series of intermittent levels of noise during JP-8 exposure (Study 4: 102dB for 15 min/hr and 1000 mg/m3). Hearing loss was assessed using the distortion product otoacoustic emission, the compound action potential, and histopathological examination of the cochlea. Results: For Study 1, a noise exposure of 85dB was identified as the lowest-observed-adverse-effect-level. Study 2 showed a dose-related increase in hearing loss greater than that seen with sound alone. The third and fourth study exposures have been completed and their analyses are in progress. Impact: Collectively, these studies will determine the effects of jet fuel exposure on NIHL and addresses the Navy Surgeon General's research priority for hearing protection. Moreover, these studies will allow a more accurate evaluation of exposure standards for the co-exposure of jet fuel and noise, leading to significant savings in health care cost and retention of specialized personnel, as well as savings to long term health care treatments to those leaving military service.

Joint Combat Casualty Research Team (JC2RT): Lessons Learned in Facilitating In-Theater Research Initiatives

Authors and Affiliations

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Abstract

The Joint Combat Casualty Research Team (JC2RT) is a CENTCOM research asset that was created to facilitate theater research efforts. All protocols to be conducted in theater, regardless of origin, must be submitted through this team for the IRB approval process. The process requires a theater approval at the Protocol Development Conference, two scientific reviews by the Institute of Surgical Research and ethical and regulatory review by MRMC. This process can be daunting, and it is one of the many challenges for investigators who desire to conduct research in the JOA. The Navy has recently joined this 10-member team, and the lessons learned from the boots on ground are important for successful Navy research in theater.

There are particular challenges to conducting research while deployed. The chaotic nature of the combat environment generally requires an observational research design. There are ethical considerations in obtaining informed consent from the injured service-member, and although it is possible to apply for a waiver of informed consent, there are certain scenarios that do not allow for this waiver. The workload of the providers does not necessarily allow for time to accomplish data collection. Many projects end up in a "failure to launch" category because of redeployment of the investigator before completion of the study and difficulty with identification of a follow-on investigator.

Keys to successful research projects include support from stateside parties who can facilitate collaborative efforts, protocol development prior to deployment, contact with the site to determine feasibility issues in advance, and research requirements, such as CITI training, completed before deployment. There are many data points that can be particularly challenging to collect such as pre-hospital care, and discussion with investigators who have experience in this type of data collection can be crucial to the success planning of the project.

Is Exercise Induced Asthma Due to a Water Channel Problem?

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Research Priorities and Gaps: Exercise induced asthma. Exercise induced bronchospasm. Water channel involvement in bronchial hyper-reactivity.

Abstract

Background: Aquaporin 5, (AQP5) is a water channel protein found in the alveolar epithelium as well as in sweat, salivary and tear gland. It is the primary determinant of membrane osmotic water permeability. Transgenic knockout mice lacking this gene exhibit pronounced methacholine induced bronchial hyperreactivity and diminished ability to produce sweat when compared to normal mice. Individuals with exercise induced asthma also exhibit enhanced airway hyper-reactivity to methacholine and diminished capacity for airway hydration. Objective: We hypothesized that exercise induced asthma (EIA) may result from a defect in AQP5 gene function. Using the muscarinic agonist-induced sweat secretion as a surrogate market for AQP5 function, we compared the subject's sweat production to their Methacholine Challenge Testing (MCT) result. Method: 56 healthy subjects, ages 18-40, evaluated for new onset exercise induced asthma, were included. The investigators were blinded to the results of the MCT. Means of the values obtained between cohorts were compared with an unpaired t-test and a p-value < 0.05 was considered to be statistically significant. Results and Statistical Analysis: Of the 56 patients, 22 were "+" and 34"-" to MCT. The mean fall in FEV1 expressed as % fall \pm SEM, were 27.9 \pm 1.6 vs. 9.0 \pm 1.1, respectively n=56, p <0.0001. Sweat secretion from the two groups expressed in mg sweat/cm2 skin/20 $min \pm SEM$ were 37 ± 3 vs. 59 ± 3, n = 56, p < 0.0001 Linear regression analysis showed a statistically significant inverse correlation between the % fall in FEV1 and sweat volumes, n=56, r = -0.59, p < 0.0001. Conclusion: Defect in the human AQP5 may help explain the diminished capacity for airway hydration that results in the bronchospasm exhibited in exercise-induced asthma.

Role of Transcranial Doppler Ultrasound in Evaluation of Patients after Traumatic Brain Injury

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Research Priorities and Gaps: Traumatic Brain Injury.

Abstract

Critical care management of patients with traumatic brain injury (TBI) has undergone tremendous advances. Neurosurgeons and neurointensivists, including military, have a large armamentarium of invasive monitoring devices available to detect secondary brain injury and guide therapy. The primary goal monitoring is to prevent secondary insults to the brain, primarily cerebral ischemia due to the posttraumatic vasospasm (PTV), and intracranial hypertension (ICH). This paper summarizes the advantages and the specific roles of transcranial Doppler (TCD) ultrasound to establish and monitor the presence of PTV and ICH.

Review of literature demonstrate that TCD is valid in predicting the patient's outcome at 6 months and correlates significantly with intracranial pressure when it is performed in the first 24 hours after the event. Recently, there have been many research results in early judgment of PTV, and TCD studies are particularly prominent in this area. The prognosis is affected severely with regard to quality of life of patients, and earlier determination of the PTV becomes very important. TCD is non-invasive, fast, and reliable as an efficient ultrasound technology, especially in critically ill patients with PTV in an urgent examination. This means that TCD has greater value and helps to improve the management of patients with TBI. Too often, the first sign is a neurologic deficit, which may be too late to reverse. However, use of TCD may predict PTV before clinical sequelae. TCD assists in the clinical decision-making regarding further diagnostic evaluation and therapeutic interventions and has become a regularly employed tool in neurocritical care. Accumulated today, experience suggests that there is an important guiding significance in early diagnosis and treatment of PTV and ICH in TCD. Because PTV and ICH represent significant events in a high proportion of patients after wartime TBI, close daily TCD monitoring is recommended for the management of such patients.

The Relationship between Mental Health Disorders and Reenlistment Status among Enlisted U.S. Marine Corps Personnel

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Research Priorities and Gaps: Post traumatic stress disorder (PTSD)

Abstract

Background: Previous research has established the link between mental health disorders such as posttraumatic stress disorder (PTSD) and unplanned personnel loss via early attrition from military service. However, the relationship between mental health disorders and reenlistment status among service members who complete their service terms and are eligible for reenlistment remains largely unknown. The relationship between mental health and reenlistment status is important because the military can potentially lose over \$60,000 each time a service member who is eligible for reenlistment does not do so. This study compared the rates of mental disorders between Marines who reenlisted and Marines who separated after one term. Methods: Medical and personnel variables used in this study were extracted from preexisting databases. Participants included 27,515 male Marines enlisting for 4-year terms between 2002-2003, including 9,338 who reenlisted after one term, and 18,177 who voluntarily separated after one term. Results: After adjusting for demographic and deployment variables, regression analysis revealed slightly higher rates of any mental disorders among Marines who voluntarily separated after one service term (odds ratio [OR]=1.2, 95% confidence interval [CI] 1.1-1.3) compared with Marines who reenlisted after one term. Of all mental health disorder categories, PTSD was the strongest predictor of reenlistment status (OR=1.9, 95% CI 1.5-2.3). Personality disorders (OR=1.8, 95% CI 1.2-2.6) and substance use disorders (OR=1.5, 95% CI 1.3–1.7) also significantly predicted reenlistment status. Conclusions: These results demonstrate that poor mental health affects retention in more ways than through unplanned loss via early discharge, including increased rates of turnover. Future studies should use these results to develop and implement targeted programs designed to increase resilience and retention of service members

Psychometric Evaluation of a Triage Decision Making Inventory

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Research Priorities and Gaps: Human injury and treatment model. Crew medical assessment.

Abstract

Background/Purpose: The primary aim of this study is evaluating the psychometric properties of the Triage Decision Making Inventory (TMDI) in a sample of active duty, reserve, and civilian nurses affiliated with a Navy military treatment facility (MTF). The TDMI measures four characteristics of triage decision making: critical thinking, cognitive behaviours, experience, and intuition. It provides a summative score of confidence in triage skills. The research gap addressed by this evaluation is the ONR gap: human injury and treatment model and crew medical assessment as triage is an essential skill in assessment of injury. Design/Methods: The TDMI was administered electronically to approximately 855 Navy and civilian nurses assigned to a MTF via an email invitation with link to Survey Monkey. Data collection took place in two sessions: April-June and October –November 2010. Results: The resulting sample consisted of 211 military and civilian nurses with various years of clinical experience and specialties. Exploratory factor analysis (EFA) using Mplus 6.1 with geomin rotation (a type of oblique rotation) was used for the k = 36 Likert scaled items. When the model was constrained to a 3-factor configuration, an interpretable solution was obtained and preliminary evidence indicates moderate support for model fit: TLI = .902, CFI = .919, RMSEA = .059 [90% CI = .052, .065] and SRMR = .041. The alpha for the instrument is .95. Three factors demonstrated acceptable reliabilities: (1) experience (.93), (2) cognitive and critical thinking skills (.92), and (3) intuition (.86). **Discussion:** A valid and reliable instrument is a source of objective data that can be linked to clinical competency and patient outcomes. It can used to evaluate training strategies in nurses who are tasked to assess human injury either in theater or in the MTF.

Funded by TSNRP (N09-001) Novice Grant Study. IRB approval: NMCSD.2009.0080. All opinions expressed in this article, report, etc. are those of the author(s) and do not necessarily reflect upon the official policy of the Bureau of Medicine and Surgery, Department of the Navy, or Department of Defense.

Patterns of Post Traumatic Stress Symptoms, Substance Abuse, and Depression among Deploying U.S. Marines

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations.

Abstract

This study explored patterns of adjustment among U.S. Marines across the deployment cycle. Active-duty USMC personnel completed an anonymous survey assessing mental, behavioral, and physical health outcomes. Participants also were asked about their place within the deployment cycle. Results yielded scant evidence for nonlinear patterns of symptom development. Overall, time until next deployment was a stronger predictor of outcomes than was length of time since last deployment. Additionally:

Those preparing for their first deployment and those who had not and would not deploy reported lower symptom levels than did combat veterans. Participants with a short deployment cycle and those who had deployed but would not redeploy reported somewhat higher symptom levels. A short deployment cycle appeared to be most strongly related to increases in substance use (e.g., heavy drinking). Correlations between the intensity of PTSD symptoms and other types of outcomes were consistently stronger for combat veterans than for nonveterans. Of all the outcomes considered, depression was most strongly correlated with PTSD. However, PTSD and depression were differentially related to deployment factors such as combat exposure and deployment cycle patterns. Substance use, including heavy drinking, illegal drug use, and tobacco use were more weakly related to PTSD symptom levels than were other outcomes, particularly depression and physical pain level. Although symptom levels tended to decrease over time following deployment, this pattern was only reliably significant for heavy drinking. Symptom levels tended to increase over time with the approach of a pending future deployment. Furthermore, the effect of time until departure on symptom levels was larger and more consistent than was the effect of time since last deployment. Results for substance use variables suggest complex patterns of influence; potential contributing factors may include military policy, social norms, and operational stress levels.

Accuracy of Rapid Prototype Models for Head and Neck Reconstruction

Authors and Affiliations

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Naval Postgraduate Dental School

Research Priorities and Gaps: Traumatic brain injury, prosthetics, and other conditions. Wound / injury management throughout the continuum of care. Warfighter restoration. Wound management.

Abstract

Purpose: To objectively validate the accuracy of rapid prototyped (RP) medical models. Materials and Methods: A dry cadaver human skull was used as the control. Stainless steel spheres (5.00mm diameter) were placed on the skull surface at seven anatomical locations and at the mid cranial fossae, as an origin for all measurements. The mechanical center of each marker was located using a coordinate measurement device and related to the origin as the control coordinate system. MDCT scan of control was interpreted by software for rapid prototyping. Six stereolithographic models were fabricated. Models were processed, cured and stored in a controlled manner, and measured using the coordinate measurement device. An Euler transformation calculation was applied to standardize the coordinate system between the control and the models. A standard t-test was used to compare the control to the models. Results: A significant difference was found at the p≤0.05. Deviations from the control were minimal in the X and Y axis; the significant differences were noted at the Z axis. However, deviations were within the size of the CT voxel dimensions. Conclusions: A coordinate measurement device was easy to use and provided objective and consistent measurements for model accuracy. The translation of the image of the control skull to the RP model is effected by the slice thickness of the CT, limitations of file software, and the rapid prototype printer. However, models were found to be accurate enough for patient planning and custom device fabrication.

Post Traumatic Stress Disorder: A Persistent Diagnostic Challenge

Authors and Affiliations

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Research Priorities and Gaps: PTSD. Human injury and treatment model (psychological injury in this case). Warfighter restoration.

Abstract

Post-traumatic stress disorder (PTSD) is unique in DSM nosology since it is the only category that clearly implies a causal agent (trauma). Early reports from the Fort Hood shootings in Texas suggested that the alleged shooter, Dr. Nidal Hassan, was suffering from an expansion of reacting to trauma. Some mental health professionals and the media attempted to connect his horrific killing of fellow soldiers to 'pre-PTSD' syndrome since he was about to deploy to the Middle East. Thus careful consideration of an individual's reaction to trauma and adversity continues to be contaminated by sensationalism and lack of critical thinking. This paper supports Treisman and McHugh, who suggest that further critical thinking is needed about this category. It will end with a review of a study which allowed for a before-and-after comparison of subjects' reactions to a traumatic experience, highlighting premorbid vulnerabilities to trauma.

Full article was published in Psychiatric Annals October 2010 issue

A Stranger in a Strange Land: Interventional Radiology in Kandahar, Afghanistan

Authors and Affiliations

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations. Advanced forward care.

Abstract

Learning objectives: Interventional radiology, a specialty that relies on high-end imaging equipment and tools, can readily adapt to the challenges of a combat hospital and provide first-world care in a third world environment. Background: In October 2009, an Interventional Radiologist was deployed to the NATO Role 3 Multinational Medical Unit in Kandahar, Afghanistan in support of Operation Enduring Freedom. In a tent and plywood hospital, using a regular operating room table and C-arm, a variety of interventional procedures were able to be performed. Procedures ranged from routine venous access to emergent pelvic arteriography and embolization in the hemodynamically unstable polytrauma patient. The integration of the interventional radiologist as a member of the operative team, in conjunction with the trauma surgeon and orthopedic surgeon, enabled us to perform multiple potentially life and limb saving procedures on the same patient during a short period of time. Clinical Findings/Procedure Details: Pictorial representation of the hospital and cases to include vertebral artery embolization, suprascapular artery embolization, pelvic embolization, profunda femoris embolization, inferior vena cava filter placement, and drainage catheter placement. Conclusion and/or Teaching Points: Interventional radiology, known and respected for unique solutions to difficult clinical problems, can and does survive and thrive in the forwarddeployed combat environment. The integration of interventional radiology into the operative team eliminates the concerns and impediments to other treatments since interventions were performed in conjunction with operative procedures.



Risk Analysis Program for Pressur Linda M. Hughes, Gail Moran, W

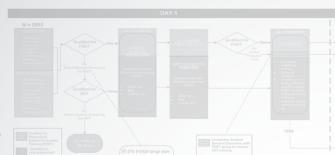


Figure 1. U.S. Navy Submarine Escape training 2 Nov 2009 – 25 Mar 2011

BACKGROUND

- Pressurized submarine escape training (PSET) prepares submariners to escape from depths of 600 feet with a submarine escape suit from a disabled submarine in cases of disaster.
- Classified as high-risk due to in-water training & low but real risk of morbidity & mortality from decompression illness, particularly AGE
- To minimize risk and adverse incidents, thoroug medical screening is done, however relevance of all components has not been firmly established
- Training commenced November 2009
- Train 2 classes per week, class size ~30

OBJECTIVES

- Develop and establish a program for data collection and risk analysis of escape training
- Examine data to determine reasons for:
 - Training pipeline washout
 - Dropout due to screening result
 - Pressure testing failure
 - 15 foot and 37 foot failures
- Determine medical incident rates and negative training outcomes
- Link outcome incidents to screening results

METHODS

- Examined throughput from 2 Nov 09 25 Mar 11
- Described student population
- Determined medical incident rates and negative training outcomes
- Identified most common reasons for pipeline washout
- Performed chi-square and Fisher's exact tests to determine if pressure test, 15 foot ascent, and 37 foot ascent outcomes were related to positive medical screening responses (significance level set at n < 05)

RESULIS

- Established data collection program
- Developed/designed: database, medical screening forms (self report Hx, physical exam, health assessments), data entry interface, and training report summaries

DEMOGRAPHICS

- 2955 male students were medically screened for PSET
- Median age 22 years (range 17-54)
- 76% enlisted/24% officers
- Assignment
 - 71% Basic Enlisted Submarine School (BESS)
 - 19% Submarine Officer Basic Course (SOBC)
 - 4% Submarine Officer Advanced Course (SOAC
 - 6% other submariners or other Nav
- Race/ethnicity
 - 78% White
 - 8% Black or African American
 - 8% Hispanic or Latin
 - 3% Asian
 - 3% other or unknown

HROUGHPUT

Medical Screening

- Figure 1 shows overall throughput, training evolution, and outcomes
- 1% of all screened were found to be unfit for any training (i.e., PSET or non- pressurized training, SET), mostly due to a sever current cold/congestion, skin condition, or medical condition
 - 57.5% were found unfit for PSET, but fit for SET (see Figure 2
- 41.5% were fit for PSET

60 Foot Chamber Pressurization Tes

 130/1225 (11%) students who qualified for the pressure test were not fit to proceed



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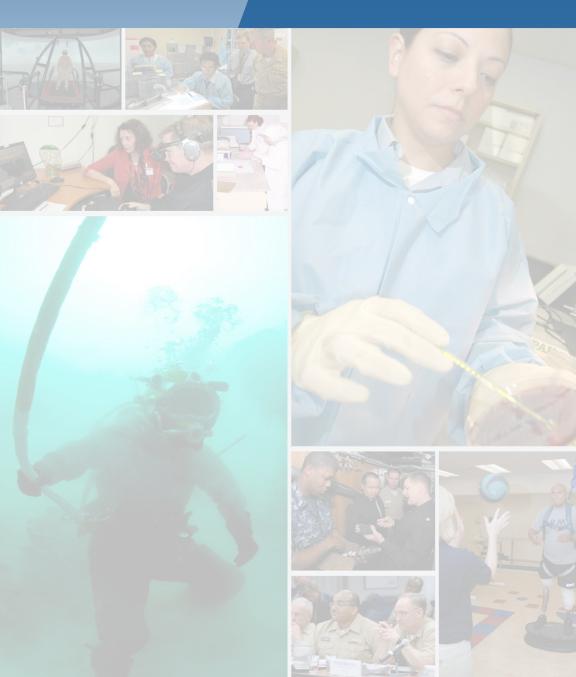
ized Submarine Escape Training 'ayne G. Horn, Seth O'Donnell







POSTER ABSTRACTS





Improved Submariner Evewear for Routine Wear and **Emergency Equipment Use Underway**

Authors and Affiliations

Alison America, MA, Wayne G. Horn, MD

Naval Submarine Medical Research Laboratory

Research Priorities and Gaps: Casualty prevention.

Abstract

New prescription eyewear for use with the Emergency Air Breathing (EAB) mask was investigated. P3 eyewear and Frames of Choice (FOC) are not compatible with donning an EAB mask. The P3 glasses cause pain in the temple region, uncomfortable temple creases, and fail to adequately fit with the EAB mask and the periscope. Frames of choice cause a break in the seal of the EAB mask, putting the submariner at risk for inhaling dangerous gases. This may cause dangerous gases to leak into the face mask, thus putting the user and crew at risk. Rochester Optical designed wire-framed eyewear (EAB17) that maintained the EAB gas tight seal.

The EAB17 was tested on three submarine crews during a 30 day to nine month underway. Users reported that the EAB17 provided a better fit with the EAB mask and with the periscope. Additionally, submariners found the EAB17 eyewear to be more comfortable and more compatible with the submarine environment compared to their usual eyewear.

What follows is an excerpt of comments from the participants:

The flexible ear hooks are far more comfortable than the P3 glasses which couldn't be worn for more than a day without being painful.

The wire framed glassed do fit inside the EAB. I can wear them in an EAB without pain like the P3. I had a positive experience with these glasses and recommend them for submarine use.

The EAB17 is a more suitable option to submariners or anyone who uses a full face mask. It ensures a tight seal with a full face mask, greater viewing with the periscope, and overall improved utility within the submarine environment. The EAB17 was clearly favoured by active duty submariners over all other options presently available.

Humanized Mouse Models for Human Diseases

Authors and Affiliations

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Research Priorities and Gaps: Tissue regeneration, prosthetics, human immune system.

Abstract

Background: Humanized mice able to reconstitute a human immune system (HIS) can be used for studies on human immunology and may provide a predictive preclinical model for human vaccines prior to clinical trials. Humanized mice may also be useful for research areas where the immune system plays a critical role, such as tissue regeneration and acceptance of prosthetics. Methods: We have generated NOD.Rag1KO.IL2RgcKO mice expressing HLA class II (HLA-DR4) molecules that were infused with HLA-DR-matched human hematopoietic stem cells (HSC), hereafter referred to as DRAG mice. Results: HSC-infused DRAG mice developed a very high reconstitution rate (>90%) with long-lived and functional human T and B cells. They also reconstituted serum levels (natural antibodies) of human IgM, IgG (all four subclasses), IgA, and IgE, comparable to humans, and elicited high titers of specific human IgG antibodies upon tetanus toxoid vaccination. Conclusions: DRAG mice develop a functional human immune system. This novel mouse strain may be useful for Navy Medical Research.

The DoD ACAM2000® Smallpox Vaccine Myopericarditis Registry

Authors and Affiliations

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations.

Abstract

Background: On March 1, 2008, a new generation FDA-approved smallpox vaccine, ACAM2000[®] officially replaced Dryvax[®]. ACAM2000[®] smallpox vaccine is a live vaccinia vaccine. Vaccinia vaccine has recently been associated with electrocardiogram (ECG) and cardiac enzyme abnormalities and occasionally with signs and symptoms associated with myocarditis and myopericarditis. Several Phase IV post-licensure studies are currently underway to evaluate the long-term safety of ACAM2000® as required by the FDA. Among the required post-licensure studies is the establishment of a myopericarditis registry to gather data among military members who have received this vaccine. Objective: Describe the ACAM2000® Myopericarditis Registry, which is designed to prospectively study the natural history of myopericarditis following receipt of the ACAM2000® vaccine, including evaluating factors that may influence disease prognosis. Methods and Results: Approximately 200 eligible subjects will be consented into the ACAM2000® Myopericarditis Registry. Enrolled subjects will be asked to complete a 20 to 40 minute survey every 6 months for a maximum of 5 years (11 surveys) if symptoms of myopericarditis persist. If symptoms do not persist, follow-up will conclude two years after the end of symptoms. Data collected will include demographic information, vaccination history, symptom history, family history as well as cardiac tests [e.g., troponin levels, electrocardiogram (ECG), echocardiogram (ECHO), magnetic resonance imaging (MRI)]. Enrollment in the Registry is ongoing. Discussion/Conclusion: The establishment of the ACAM2000 Myopericarditis Registry ensures the continued licensure of this military relevant vaccine and could lead to policy modifications, such as enhancements to pre-vaccination screening, to further safeguard the health of service members.

Identification of Next-Generation In-Cockpit Oxygen Sensors to **Reduce Hypoxia-Related Casualties**

Authors and Affiliations

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Research Priorities and Gaps: Casualty prevention.

Abstract

Introduction: Hypoxia is the number one physiologic threat to naval aircrew, representing a substantial loss of equipment, mission hours, and aircrew lives. Several operational reviews identify the need for incockpit monitoring to alert pilots to the onset of hypoxia before flight safety is compromised. The current clinical standard for oxygen monitoring, pulse oximetry, has significant sensor placement constraints and lacks the ability to accommodate hemodynamic variability during flight, making the technology unsuitable for use in aviation environments. Purpose: To explore new, more viable technologies aimed at preventing hypoxia-related casualties. Current evaluations: Our laboratory evaluated foreheadmounted near-infrared spectroscopy (NIRS) and reflectance oximeters as potential hypoxia detection tools. Both sensors were found to respond to changes in oxygen concentration as quickly as pulse oximetry, although both technologies possessed weaknesses. Reflectance oximeters were highly susceptible to motion artifact often resulting in complete signal loss. NIRS sensors were less susceptible to motion; however, readings depended on sensor placement, and inter-person variability made establishing detection thresholds difficult. Future evaluations: Recent sensor advancements utilizing nano and terahertz technology may pave the way for quick and reliable methods to detect impending hypoxic events. Newly developed fiber-optic-based sensors, which directly measure the partial pressure of oxygen, could be incorporated into flight masks to monitor breathing air content. Smart textiles are being developed, combining electronics and conductive fabrics to sense vital signs. Incorporating oxygen sensing into these fabrics may provide a seamless option for monitoring. Another innovative approach is breath analysis, potentially allowing for continuous physiologic monitoring across an array of biological indices. Future research will explore the validity and practicability of such emerging sensor technologies for operational use. This research is aimed at filling the Office of Naval Research gap of casualty prevention in the aviation arena.

Aviation Casualty Prevention through Applied Spatial Disorientation Research

Authors and Affiliations

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Research Priorities and Gaps: Casualty prevention.

Abstract

Pilot spatial disorientation (SD) is the leading aeromedical factor contributing to Navy class A flight mishaps. Across the services, SD-related mishaps result in average annual losses of 25 lives and \$400 million in aircraft. To address this significant threat to pilot safety and operational effectiveness, NAMRU-Dayton is leading the Navy's reinvestment in research to identify causes of, and countermeasures for, pilot SD. Core NAMRU-Dayton research capabilities in the visual, vestibular, and cognitive sciences are supported by a unique collection of state-of-the-science, motion-based research devices.

NAMRU-Dayton's human-rated motion platforms include the Disorientation Research Device (DRD Hercules), the Visual Vestibular Sphere Device (VVSD), the Vertical Linear Accelerator (VLA), and the Clinical Vestibular Rotator (CVR). Each device is capable of unique motion profiles affording independent control of visual and vestibular stimuli to isolate sensory interactions associated with SD in flight.

The DRD Hercules combines a precisely controlled six degree-of-freedom acceleration environment, with dynamic visual displays to recreate and evaluate environments associated with SD during flight. The VVSD provides rotation of subjects within an independently controlled, completely immersive spherical surround to study sensory spatial reflexes and spatial awareness related to stabilization of retinal images. The VLA is capable of executing precise linear motions along a long vertical track, which can synchronize with a visual display to recreate stimuli associated with SD episodes experienced during helicopter flight such as "brownout." The CVR provides earth- and off-vertical rotation within an independently controlled visual field to study visual and vestibular interactions, which can cause loss of spatial awareness.

These research devices support a range of basic and applied research from basic physiology to testing of spatial awareness-enhancing display principles. Ultimately, these capabilities enable NAMRU-Dayton to transition validated knowledge and effective technologies to the fleet that will reduce and prevent casualties caused by SD.

Prevalence and Auditory Effects of Blast-Related Ear Injury in Operation Iraqi Freedom

Authors and Affiliations

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Naval Health Research Center

Research Priorities and Gaps: Hearing protection and restoration. Wound / injury management throughout the continuum of care. War fighter restoration.

Abstract

The auditory effects of blast-related ear injury are a primary concern in the deployment environment because they can compromise a service member's situational awareness and impact operational readiness. In addition, hearing loss and tinnitus are among the top service-connected disabilities, with more than \$1 billion spent in 2006 to compensate veterans. The objective of this analysis was to describe the occurrence of blast-related ear injury during Operation Iraqi Freedom (OIF), identify the impact of hearing protection at the point of injury, and explore long-term auditory outcomes. The Expeditionary Medical Encounter Database (EMED) was used to identify service members who survived blast-related injury during deployment in OIF (n=3981). The EMED data were linked with outpatient medical databases to obtain auditory ICD-9-CM diagnosis codes. The prevalence of ear injury was 30.7% (n = 1223). The most common ear injury diagnoses were "inner or middle ear injury involving tinnitus" (n=767) and "tympanic membrane rupture" (n=319). Hearing protection was found to only have a protective effect against "inner or middle ear injury involving tinnitus" (p<0.001). Hearing loss was the most frequently reported auditory disorder diagnosed after injury (11.5%). Blast-injured service members with "tympanic membrane (eardrum) rupture" had higher odds of hearing loss (odds ratio = 6.90, 95% confidence interval, 5.20-9.15). "Inner or middle ear injury involving tinnitus" was not associated with hearing loss. Ear injury is a frequent consequence of blast exposure. Although hearing protection is warranted for all service members at risk of blast exposure during combat deployment and may mitigate ear injury involving tinnitus, it does not appear to protect against tympanic membrane ruptures, which were associated with hearing loss outcomes. These injuries should be closely monitored in-theater and throughout the continuum of care in order to identify hearing-related morbidity that can impact service members' operational readiness.

Assessing Intra-individual Variability after Traumatic Brain Injury **Using Grip Force Dynamometry**

Authors and Affiliations

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Research Priorities and Gaps: Traumatic brain injury (TBI). Advanced forward care

Abstract

Introduction: Intra-individual variability (IIV) is typically measured using simple reaction time tasks. IIV is increased in dementia, stroke, and trauma. Motor control is known to be subtly disordered even after lesions distant from primary motor areas. Grip dynamometers, sampling at 1000 Hz, allow measurement of variability of grip force. We have previously demonstrated that grip force variability in the unaffected side after stroke can distinguish between persons with stroke and uninjured age-matched controls. We present an ongoing study to examine the utility of grip force IIV in TBI screening. Methods: We are assessing 35 civilians (ages 17-55 years) with medically confirmed and symptomatic mild or moderate TBI within 6 months. Controls are matched for age, gender, and education. Subjects are tested in the seated position, and view visual feedback regarding grip force produced. Target range is between 5% of norm and 5% plus 0.25 lbs, sustained for 4 min. An instrumented grip dynamometer (G100, Biometric Ltd, sampling frequency 1000 Hz) collects data, and custom software (Matlab) presents feedback about current force and target ranges on a computer screen. We currently define IIV as 1) seconds outside target range (time); 2) SD of grip force (force); 3) summed rectified difference from own mean generated force (force × time); and 4) summed rectified error outside target range (force × time). Receiver Operating Characteristic (ROC) curves will be used to compare the performances of the four IIV definitions in terms of true positive (sensitivity) and false positive (1-specificity) rates. Results: Feasibility data on first subjects will be presented. Discussion: IIV, a measure of neurobiological health and functioning, is known to be increased in brain disorders including trauma. If grip force dynamometry discriminates persons with mild/moderate TBI from controls, it may be a TBI screening tool useful in forward deployment.

Visual Performance and Hypoxia: A Dual Threat to Aviator Safety

Authors and Affiliations

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Research Priorities and Gaps: Restoration of sight and eye-care. Casualty prevention.

Abstract

Introduction: The effect of hypoxia on physiological function is well understood, but the full extent to which hypoxia affects visual performance, and other related systems, has not been well elucidated. Visual processes such as visual acuity, contrast sensitivity, color perception, and peripheral vision play an obvious critical role in aviator performance, but vision also plays a substantial role (80%) in maintenance of situational awareness and orientation; the loss of which contributes to more casualties and loss of life in aviation than any other mishap causal factor. To address this gap and determine future hypoxia research directions, a systematic search of all English-language articles in PubMed was performed. Method: Forty-eight articles published between 1923 and 2010 were reviewed. Several conclusions pertinent to aviation-relevant visual performance were drawn. Results: Rod-mediated scotopic visual acuity is degraded by hypoxic exposure above 10,000 feet (ft), while cone-mediated photopic vision is largely unaffected until altitudes exceed 18,000 ft. Hypoxia causes degradation in both spatial and temporal contrast sensitivity, particularly under dim light. Furthermore, at higher simulated altitudes (≥25,000 ft), mean visual sensitivity across the visual field is significantly reduced, particularly in the peripheral visual field. With regard to color vision, most studies lacked testing across a wide color spectrum, and therefore, agreement has not been reached regarding which colors are most affected by hypoxia. Lastly, hypoxia appears to cause a rapid onset of degradation in visual accommodation and a loss of convergence. Overall, the magnitude of hypoxic effects on ocular functions co-varies with altitude and luminance levels. Conclusion: The review clearly reveals significant gaps in our understanding of hypoxia's mechanisms of action and extent of effect on visual factors such as color vision and pupil size and function. Clarifying these mechanisms may lead to improvements in Night Vision Goggles, Heads-Up Displays, and cockpit design and development.

Influence of Acute Vestibular Impairment Following Mild Traumatic Brain Injury on Subsequent Ability to Successfully Complete a Vestibular Physical Therapy Program and Remain on Active Duty One Year Later

Authors and Affiliations

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Research Priorities and Gaps: Wound management. Advanced forward care. Mitigation and treatment of traumatic brain injury neurotrauma.

Abstract

Introduction: Mild traumatic brain(mTBI) injury secondary to blast exposure is a significant operational issue and a rising international concern in modern society. This abstract describes the vestibular/visual/cognitive (VVC) patterns seen in these patients before, after, and one year following vestibular physical therapy (VPT) treatment. Objective: To investigate the relationship of VVC tests and the computerized dynamic posturography sensory organization test and the ability to remain on active duty status in the US military following VPT rehabilitation. Methods: Among our group of 82 blast patients with vestibular dysfunction who responded to VPT, forty-seven mTBI individuals were available one year later for long term objective follow-up. Utilizing the "In-vision" tunnel we performed several VVC tasks to include static visual acuity, perception time, target acquisition, target following, dynamic visual acuity (DVAT), and gaze stabilization (GST). Utilizing computerized dynamic posturography we performed the sensory organization test (SOT). Results: All baseline (income) test scores were compared to outcome scores taken 12 weeks and one year after completing VPT. DVAT, target following, target acquisition, and perception time normalized within twelve weeks, whereas GST did not normalize until after 12 weeks of vestibular physical therapy. SOT function normalized in all patients and this normalization was maintained in long term follow-up. Conclusions: This set of VVC tests appear reasonable to establish initial status and to evaluate progress associated with participation in VPT. At the current time we can show significant improvement and normalization for target following and DVAT testing scores. GST was the most likely score to deteriorate over time. One year after VPT treatment, some of the benefits of vestibular rehabilitation are not maintained in a subgroup of these patients. We describe the characteristics of this subgroup and conclude that maintenance therapy or challenged vestibular actively is an important adjuvant to initial vestibular rehabilitation.

Comparison of Cone Beam CT and Conventional CT in Accuracy of Rapid Prototype Models: Image Registration

Authors and Affiliations

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Research Priorities and Gaps: Traumatic brain injury. Prosthetics. Wound / injury management throughout the continuum of care. War fighter restoration.

Abstract

Purpose: Validate the use of captured images from the Cone Beam Computerized Tomography (CBCT) for accuracy by comparing them to conventional CT images (gold standard) for use with Rapid Prototyping of models and treatment planning software and applicability for registration of images. **Methods:** A standard model was developed by adding fiducial markers (5mm stainless steel balls) at anatomical landmarks on a human skull. The model was then acquired by the Iluma CBCT scanner (Imtec, Ardmore, OK), at 7.8s, 20s, 40s and by a Philips Brilliance 40 (Philips Healthcare, Andover, MA). Distances between fiducial points and the markers were determined using rapid prototype software (Magic RP). Differences between the absolute value of differences between the conventional CT and CBCT images taken at 3 different speeds were compared for accuracy. Statistical analysis was performed using a multivariate analysis of variance (MANOVA, α=0.05). **Results:** The MANOVA analysis did not detect significant differences between spatial deviations in the CBCT scans at different exposures. **Conclusions:** These results imply that CBCT scans can yield similar 3-D spatial accuracy to MDCT scans in craniofacial modelling accuracy and registration of Cone Beam CT to MDCT to account for missing information for reconstruction.

Retinoid Signaling by a Selective Retinoid Acid Receptor Agonist Hinders Angiogenesis: Formation of Granulation Tissue and Wound Closure in **Cutaneous Models of Wound Healing**

Authors and Affiliations

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Research Priorities and Gaps: Wound/injury management throughout the continuum of care. Other conditions directly relevant to injuries on the battlefield.

Abstract

Background: Heterotopic ossification (HO) is a common late complication of modern wartime extremity injuries. Recently, the prophylactic administration of retinoid acid receptor agonists (RARA) was found to inhibit the formation of heterotopic ossification, thought in part to inhibition of vascular development. The effects of RARA on tissue revascularization and cutaneous wound closure are unclear. The aim of our study is to determine the effects of RARA treatment in murine models of wound healing on skin isograft revascularization and acute excisional wounds. Methods: A circular 2 cm² full thickness excisional wound was produced on the dorsum of adult female BALB/C mice. Wounds were either left open or covered immediately with a full-thickness syngeneic skin graft. Mice were treated daily with RARAγ or vehicle control for 7 days. Grafted skin was assessed at different time points for gross revascularization, angiogenic mRNA transcript expression, CD31⁺ vessel density, and histology. Open wound areas were quantified using digital planimetry. Results: In comparison to vehicle-treated mice, a marked loss in skin isograft integrity and graft revascularization was observed at the macroscopic level in grafts from RARAy-treated mice at day-7. RT-PCR gene expression of grafts and wound margin tissue revealed marked suppression in a number of key proangiogenic gene transcripts including: angiopoietin, chemokines, proinflammatory cytokines, FGF6, MMP9 and leptin (p < 0.05). Moreover, histological analysis indicated decreased graft re-epithelialization as well as a 32% reduction in wound bed granulation tissue containing 73% fewer CD31⁺ vessels per hpf. RARAγ treatment strongly delayed open excisional wound closure as a result of reduced granulation tissue formation and impaired wound contraction. Conclusion: Although RARA have shown effectiveness against HO formation, our results reveal a suppressive regulatory role of retinoid signaling on key wound healing processes and may dampen enthusiasm for HO treatment in the setting of open fractures.

Benchmarking to the International Pressure Ulcer Prevalence Survey

Authors and Affiliations

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Abstract

Purpose: To obtain data regarding prevalence and incidence of pressure ulcers in our agency, and compare those data to national benchmark data as a basis for improving our wound care protocols. Subjects and Setting: Health care facilities throughout the nation volunteered to participate in the data collection process for a multiday pressure ulcer prevalence survey performed in February 2009. Each facility collected prevalence data during a pre-selected 24-hour period out of the 72-hour time frame selected by the national study. The authors and team members from the Naval Medical Center at Portsmouth, Virginia participated in this study. Methods: Demographic information, pressure ulcer stages, locations, pressure redistribution surfaces, and Braden Scale assessment comparison were collected and submitted to a central site for database entry, analysis, and generation of reports. Results: The pressure ulcer incidence of adults managed in acute care inpatient units at Naval Medical Center Portsmouth (NMCP) was 6.6% and the prevalence was 10%. The most common location of facility acquired pressure ulcers at NMCP was the heels (50%). Conclusions: Benchmarking is a tool that allows health care professionals to compare outcomes in their agencies to outcomes in comparable facilities. Identification of areas in which agency outcomes compare negatively to benchmark data should prompt implementation of quality improvement initiatives. National pressure ulcer prevalence surveys provide a benchmark to evaluate an individual facility's care and treatment of patients at risk for pressure ulceration. The true benefit of participation in such surveys, however, is determined by local health care professionals' ability to use national data to improve clinical practice.

Risk Analysis Program for U.S. Navy Submarine Escape Training

Authors and Affiliations

Linda M. Hughes, Gail Moran, Wayne Horn

Naval Submarine Medical Research Laboratory

Research Priorities and Gaps: Undersea medicine. Diving and submarines.

Abstract

Introduction: Pressurized Submarine Escape Training (PSET) is classified by the U.S. Navy as highrisk, due to in-water training and the risk of morbidity and mortality, particularly from arterial gas embolism. Given the student throughput of over 2000 students a year and previous U.S. and foreign navy experience, training incidents are a certainty. Risks are minimized through medical screening; however, the effectiveness of some screening components has not been firmly established. The primary objective of this project was to provide the submarine training leadership, trainers, and undersea community with a risk analysis program to investigate and validate medical screening procedures and techniques and better identify training risk factors at the new U.S. Navy submarine escape training facility. Methods: A program for data collection and risk analysis of the escape training experience was developed. Medical incident rates and negative training outcomes were determined and relationships between incidents and negative training outcomes and screening results were examined. Results: During the initial year (2 Nov 2009 to 3 Nov 2010) of PSET 2,147 students were screened, mostly from Basic Enlisted Submarine School. Of these, 32% of students received PSET, 66% received non-pressurized submarine escape training (SET), and 2% did not receive any training. The most common reason for PSET disqualification was congestion or a current cold. During pressure testing and the 15 and 37-foot ascents, the most common medical incidents were ear barotraumas. No significant (p < .05) relationships were found linking any of the screening results to pressure test outcomes. The only relationship found between screening results and 37-foot ascent outcomes was smoking behavior. Thirty-five percent of the students who experienced some type of medical incident during their 37' ascents were smokers compared to a smoking rate of 19% among those who successfully completed the 37' ascent, ($\chi^2_3 = 6.5$, P = .01). There were too few cases to examine relationships between 15-foot medically related ascent incidents and screening results.

Burn Pit Smoke Exposure and Health Risks in the Millennium Cohort Study

Authors and Affiliations

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Research Priorities and Gaps: Other conditions directly relevant to injuries on the battlefield.

Abstract

Introduction: Recent media and Veteran concern has focused attention on the potential health impact to military personnel from potential exposures emanating from open-air burning of trash and other waste in theater. The objective of this study was to investigate the association between possible smoke exposure from documented open-air burn pits and three distinct groupings of symptoms or illnesses: 1) a continuum of symptoms aggregated to define chronic multi-symptom illness, 2) immune dysfunction measured by new-onset lupus and rheumatoid arthritis, and 3) respiratory illnesses defined by persistent or recurrent cough or shortness of breath, new-onset chronic bronchitis or emphysema, and new-onset asthma. Methods: The study population consisted of Army and Air Force participants from the Millennium Cohort Study who completed both 2004-2006 and 2007-2008 questionnaires and deployed in support of the current operations in Iraq and Afghanistan between 2003 and 2008. Using data from three different camp sites in Iraq with documented burn pits, three measures for burn pit exposure were assessed: proximity near a burn pit, cumulative days at a camp site, and deployment by camp site. Results: Of the 18,000 deployers, more than 3,000 deployed within a 3-mile burn pit radius. Those who deployed within a 3-mile proximity of a burn pit did not have increased odds of any of the outcomes (p >0.05) after adjusting for demographic, military, and behavioral characteristics. However, after adjustment, those exposed at Joint Base Balad had increased odds of new-onset lupus (p = 0.025), although there were only 2 cases at this site. Conclusions: Overall, these findings are reassuring that deployers possibly exposed to documented burn pits in the combined three-camp analysis were not at elevated odds of chronic multisymptom illness, new-onset lupus and rheumatoid arthritis, and respiratory illnesses. More detailed exposure data are needed to further evaluate the potential health risk of burn pit exposures.

The New Zealand Breacher Study: Blood Brain Biomarkers, Neuro-Cognitive **Performance and Self-Reported Symptoms**

Authors and Affiliations

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Research Priorities and Gaps: Traumatic brain injury and post-traumatic stress disorder.

Abstract

Objectives: 1) Identify and validate the sensitivity of several mild brain injury protein markers detected in blood samples from subjects exposed to repeated low level blast during a two week explosive entry training course (New Zealand Breacher Study); 2) Correlate neurocognitive performance (ANAM4 TBI Battery) and subjective symptom data with serum biomarker data. Methods: This Phase 1 project analyzed the concentration of five candidate biomarkers (SBDP150, UCH-L1, MAP2, GFAP, ICAM, NCAM) in 24 serum samples collected from 19 volunteers prior to, during, and seven and 14 days following a two-week explosive entry course. Each volunteer completed the Automated Neurocognitive Assessment Metric (ANAM) battery and a symptoms questionnaire commensurate with serum samples at the end of each day. One way repeated measures analysis of variance (ANOVA) using SAS GLM procedure and SAS MIXED procedure and cluster analyses were used to classify potential subclinical effects among trainees. Rank scores were assigned to each trainee. The most and least affected trainees with respect to biomarkers and ANAM performance were subjected to additional analysis. Results: Significant group mean differences were identified for GFAP (P=0.0114) and in the ANAM tasks mathematical processing (MTH, P=0.0235) and simple reaction time (SRT2, P<0.0093). Five out of the seven most affected trainees, according to rank scores among biomarker tests (UCH-L1, SBDP150 and GFAP), overlap with five out of the six most affected trainees according to ANAM performance. In addition, symptoms associated with blast exposure (e.g. headache), as opposed to fatigue, also appear to be associated with blast exposure and ANAM performance. Conclusions: Mild traumatic brain injury (mTBI) as a result of blast exposure can be hard to diagnose. These data suggest that there is a relation between a number of candidate blood biomarkers, deficits in neurocognitive performance, and self-report of negative symptoms that follow exposure to low-level blast.

Extra Amniotic Balloon for Pre-Induction Cervical Ripening: A Randomized Comparison of Weighted Traction vs. Non-Weighted

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations.

Abstract

Objective: To determine whether a weighted vs. non-weighted extra-amniotic supracervical balloon catheter achieved a shorter first stage of labor in the cervical ripening of an unfavorable cervix. Methods: This was a randomized trial of patients presenting to Naval Medical Center Portsmouth for labor induction with an unfavorable cervix (Bishop score <4). Women were randomized to one of two groups: weighted balloon catheter with 1,000 mL fluid bag and non-weighted with the balloon catheter taped to the patient's thigh. Results: A total of 62 women were randomized to the weighted vs. non-weighted balloon catheter groups. Time from balloon discontinuation until complete dilation was not different in the weighted 817.5 ± 55 minutes vs. non-weighted group 838.2 ± 57 minutes (p=0.7972). The time from balloon catheter insertion until discontinuation was significantly longer in the non-weighted group 277 ± 39.1 vs. 95.6 ± 11.9 minutes in the weighted group (p=0.001). This resulted in longer cervical ripening / first stage of labor in the non weighted 1111.0 ± 57.6 vs. weighted group (p=0.0246). The non-weighted balloon catheter had a shorter first stage of labor as gravidity increased (p-0.007) and as race went from white to non-white (p = 0.0028). Conclusions: The first stage of labor after cervical ripening is not shortened by a weighted balloon catheter. The total time from cervical ripening to the end of the first stage of labor is significantly shortened with the weighted balloon catheter. Both gravidity and race interact with the weighted balloon catheter to shorten the first stage of labor.

Non-combat Motor Vehicle Accidents during Operation Iraqi Freedom

Authors and Affiliations

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Research Priorities and Gaps: Wound / injury management throughout the continuum of care. Advanced forward care. Casualty prevention.

Abstract

During current wartime operations, a vast majority of injuries are the result of non-battle incidents. Motor vehicle accidents (MVA) are one of the leading causes of non-battle injury, and can often lead to injuries severe enough to require evacuation from theater. Detailed analysis of MVA incidents is often not possible due to missing information. The aim of the present study was to describe the patterns and correlates of injuries sustained in non-combat MVAs during Operation Iraqi Freedom. Clinical records for 348 individuals injured in incidents of non-combat MVA (E-code 810-825) between March 2004 and February 2008 were identified from the Expeditionary Medical Encounter Database. Injury Severity Score (ISS) was coded for all personnel. The most common mechanism of MVA was non-collision due to loss of control (30%), with this mechanism also accounting for 90% of all rollover incidents. Injuries to the extremities (68%) and head, neck and face (34%) were most common, though torso injuries accounted for 61% of all severe injuries. Overall, 14% of individuals sustained fractures, with fractures more prevalent in rollover incidents compared to non-rollover (23% vs. 12%). Rollover incidents were also associated with a higher ISS compared to non-rollovers, had a higher percentage of spine/back (38% vs. 18%) and torso (27% vs. 10%) injuries, and were more likely to be medically evacuated (39% vs. 26%). Drivers and passengers suffered the highest rates of head, neck and face injuries (50% and 41%, respectively), while gunners and pedestrians had the highest rates of extremity injuries (90% and 87%, respectively). Injury severity did not differ significantly by position in vehicle. This analysis provides a thorough analysis of non-combat MVAs and provides a foundation for further research. Future studies should incorporate detailed accident reports to identify potential mitigating factors of injury severity.

Trends in Post-Concussive Symptom Reporting Following Mild Traumatic Brain Injury in Operation Iraqi Freedom

Authors and Affiliations

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Research Priorities and Gaps: Traumatic brain injury. Mitigation and treatment of neurotrauma. Wound / injury management throughout the continuum of care.

Abstract

Post-concussive symptoms frequently occur following mild traumatic brain injury (TBI). Research in civilian populations has demonstrated that a majority of these symptoms resolve within the first 90 days post-injury. Little is known, however, regarding symptom trends following combat-related TBI. The Expeditionary Medical Encounter Database was queried for all provider diagnosed TBI and non-TBI between 2004 and 2008 who completed a post-deployment health assessment (PDHA). Because a TBI event can occur at any time during a deployment, personnel can answer a PDHA anywhere from days, weeks to many months after injury. Personnel were categorized into those responding to a PDHA less than 3 months (n = 386 TBI, 1332 non-TBI), 3-6 months (n = 382 TBI, 1074 non-TBI), and 6-12 months (n = 88 TBI, 378 non-TBI) from the time of injury. Symptom complaints on the PDHA were examined and all multivariate analyses were adjusted for age, injury severity, combat exposure, post-traumatic stress disorder, and blast mechanism. The analysis yielded differing post-concussive symptoms for each of the PDHA response periods. In the first 3 months following injury, those with TBI had significantly higher odds of headache, back pain, and memory problems compared to non-TBI. In the 3-6 month period, only headache was significantly higher in TBI than non-TBI. Finally, in the 6-12 month period, there was a higher odds of headache complaints in TBI compared to non-TBI, as well as memory problems, back pain, and sleep complaints. These findings suggest post-concussive symptoms change over the course of one-year following combat-related TBI. These symptoms, particularly in the early stages following TBI, may affect operational performance. The association between TBI and health complaints 6-12 months following TBI may be a result of impeded recovery due to continued presence in a stressful environment, and warrants further study with a larger sample size.

Perfluorocarbon Treatment of DCS

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Research Priorities and Gaps: Human injury and treatment models. Casualty prevention. Warfighter restoration.

Abstract

Background: Non-recompressive therapies for DCS to support DISSUB rescue are needed. The size, gas carrying capabilities and surfactant properties of perfluorocarbons (PFC) make them ideal candidate drugs. PFCs appear beneficial in preventing DCS, but have not been studied as therapeutic agents. Developmental barriers include lack of FDA approval and uncertain safety. NMRC/UMD is investigating PFC therapeutic efficacy in animal models and collaborating with NEDU to establish safety guidelines for human use. This may allow for FDA approval using the "two-animal rule" when human efficacy experiments are not feasible. Methods: Severe DCS in swine: After 200 fsw/31 min and DCS onset, 20kg swine are randomized to 5 cc/kg of Oxycyte (PFC) or Saline (with surface oxygen). Primary endpoints: mortality, abnormal gait. PFC and TT6: Swine fitted with EEG electrodes are dosed with 5cc/kg of PFC 12h prior to a Navy TT6; monitored for seizure occurrence. Seizure latency and duration: Animals randomized to 5cc/kg PFC or Saline, fitted with a nose cone and surface electrodes and compressed to 165 fsw on air, observed for 2 min, then the breathing gas switched to Oxygen. EEG, EKG, and videography data are collected. Seizure onset defined as spiking waveform activity combined with generalized convulsions. Breathing gas returned to Air upon seizure onset; same animal exposed to same profile 24 h after original infusion. Rat PFC Therapy: Tail veins cannulated; animals compressed to 210 fsw/60 min then rapidly decompressed. Upon DCS onset animals are given 100% surface oxygen and randomized to 5cc/kg PFC or Normal Saline. Endpoints (mortality, gait at 24h) are being analyzed. Tissues collected, perfuse-fixed brain and spinal cord. Results: 5cc/kg PFC + oxygen after DCS onset significantly decreased mortality; 3cc/kg PFC does not decrease mortality (spinal histology is being analyzed). 5cc/kg PFC does not decrease latency (p=0.81) or duration (p=0.12) of seizure; Oxygen 1H and 24H after infusion. Summary: Treating severe DCS with intravenous PFC is examined in two animal models. The effect(s) of PFC on seizure risk during hyperbaric oxygen will facilitate human safety studies.

Perfluorocarbon (PFC) Administration Decreases Mortality in a Rat Model of Decompression Sickness

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Research Priorities and Gaps: Casualty prevention.

Abstract

Introduction: During diving, inert gas such as nitrogen accumulates in the body. In an emergency, such as escaping from a disabled submarine that is flooding or running out of oxygen, these inert gases can come out of the tissues causing decompression sickness (DCS) or the bends. Severe DCS is generally manifested as cardiopulmonary compromise or neurologic injury. Cardiopulmonary compromise is likely the result of a severe violation of a decompression schedule. Such a scenario has occurred in diving mishaps and is likely in a disabled submarine rescue. Neurologic DCS comprised 40% of recorded cases in a civilian database and contribute most frequently to morbidity associated with diving. It has been shown that PFC administration with 100% oxygen for 1 hour after DCS onset improved survival in a 20kg swine model (2). This study tested the hypothesis that perfluorocarbon (PFC) administration + 30 minutes of 100% oxygen delivery would improve survival in a 260g (± 10g) rat model of DCS. Methods: After rapid decompression from 60 minutes at 210 fsw (7.4 ATA) animals were observed for signs of DCS. Animals that experienced DCS were randomized to receive 100% O2 (30 min.) + Saline or 100% O2 (30 min.) + PFC. After 24 hours, the primary outcome of mortality was assessed. Results: Efficacy of combined PFC and Oxygen therapy for DCS was analyzed for significance. A reduction in mortality rate was observed where 33/58 (56.9%) of oxygen + saline treated animals and 28/68 (41.2%) of oxygen + PFC treated animals were non-survivors at 24 hours. This resulted in a relative reduction in mortality between saline and PFC treated animals of 27.6% (p < 0.05; Chi-square test for statistical significance, one-sided). Conclusions: PFC and 30 minutes of O2 administered after DCS onset decreased mortality in this 260 g rat model. This study lends further evidence for potential benefit of PFC as a therapy for treatment of DCS. Further studies into mechanisms and benefit are warranted.

The Role of Military Occupation on New-Onset Posttraumatic Stress Disorder and Depression Diagnoses among Personnel Deployed to Iraq

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Research Priorities and Gaps: Post-traumatic stress disorder. Casualty prevention.

Abstract

Objective: We examined the role military occupation has on new-onset posttraumatic stress disorder (PTSD) and depression among personnel deployed to Iraq. Methods: The study population consisted of 40,600 Navy and Marine Corps personnel without history of mental health disorder prior to deployment. We assessed these personnel for new-onset PTSD and depression diagnoses within a year after returning from deployment to Iraq. Multivariate logistic regression was used to examine the association between occupation and post-deployment PTSD and depression diagnoses by branch of service. Analyses were adjusted for combat injury and demographic variables. Results: Navy health care specialists had higher odds of new-onset PTSD (odds ratio [OR]=4.53; 95% confidence interval [CI]=2.58, 7.94) and depression (OR=2.58; 95% CI=1.53, 4.34) compared with Navy functional support/other personnel. In addition, Marine combat specialists had higher odds of new-onset PTSD (OR=1.91; 95% CI=1.48, 2.47) and depression (OR=1.36; 95% CI=1.10, 1.68) compared with Marine functional support/other personnel. Marine Corps service and supply personnel were also more likely to be diagnosed with PTSD (OR=1.72; 95% CI=1.29, 2.29). In an additional analysis, a larger percentage of Navy health care specialists than Marine Corps combat specialists were diagnosed with PTSD (6.3% versus 4.1%) and depression (5.2% versus 4.2%). Conclusion: Occupation plays a significant role in the development of new-onset PTSD and depression. The high rates of PTSD and depression among health care specialists warrant further investigation into the potential effects of caregiver stress on mental health.

Profile of Pediatric Admissions to the USNS Comfort Following the 2010 Haiti Earthquake: Lessons for Future Hospital Ship Based Disaster Relief Missions

Authors and Affiliations

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations. Wound / injury management throughout the continuum of care.

Abstract

Objective: To profile the types of pediatric admissions to the USNS COMFORT during Operation Unified Response Haiti (OUR-H) and present recommendations for pediatric staffing on future hospitalship based disaster relief missions. Design: A retrospective chart review. Settings: USNS COMFORT Hospital Ship off the coast of Port-au-Prince, Haiti during the Haitian earthquake disaster relief mission. Participants: All patients 0–17 years old admitted to the USNS COMFORT between January 20, 2010 and March 15, 2010. Main Outcome Measure: Age distribution of admissions, types and causes of injuries, number requiring surgical intervention, time to first surgery and number and type of admissions to the combined NICU/PICU and average length of stay were recorded. Results: Of 787 total humanitarian admissions, 224 (28%) were pediatric patients with 69% (156) directly quake related and 167 (75%) classified as trauma. Surgery was required for 122 (54%) with the first procedure occurring in one day or less for the majority (68%) of these. The majority of PICU admissions (54%) were secondary to non-quake related diseases. The average length of stay was not significantly different between quake and non-quake related admissions, excluding patients born aboard, although the average age was at 8.7 years and 6.2 years respectively. Conclusion: The mission's primary goal was surgical but a significant minority of pediatric patients admitted did not require surgery or were non-trauma related diseases or births requiring medical management. The arrangement of pediatric providers as hospitalists contributed to the minimal delay seen from time of admission to initial surgical procedure despite the rapid influx of patients. Future disaster related USNS COMFORT missions must plan for sufficient pediatric providers, intensivists and nurses to manage both medical and surgical patients.

A Comparison of the Prophylactic Combination of Palonosetron and Dexamethasone versus Ondansetron and Dexamethasone on the Incidence and Severity of Post-discharge Nausea and Vomiting in a Group of High Risk Patients

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Research Priorities and Gaps: Other conditions directly relevant to injuries on the battlefield. This study addresses issues directly affecting the comfort of those sailors and soldiers after discharge from the hospital.

Abstract

Introduction: Palonosetron, the most recently FDA approved 5-HT3 receptor antagonist for the treatment of PONV, has an elimination half-life of 40 hours. Currently, patients at high risk for PONV receive prophylactic treatment with ondansetron, a 5-HT3 receptor antagonist, and dexamethasone. The prophylaxis provided by this regimen, however, is limited by ondansetron's short elimination half-life of 5.7 hours. Palonosetron may provide prophylaxis in the post discharge period for up to 72 hours. To date, there are no published studies comparing the combination of ondansetron and dexamethasone to palonosetron and dexamethasone for the prophylactic treatment of PONV. The purpose of this study was to examine efficacy of palonosetron and dexamethasone versus ondansetron and dexamethasone in the prevention of PONV and post discharge nausea and vomiting (PDNV). Methods: Eighty-four females identified as high risk for PONV, undergoing general anesthesia, were approached for enrollment in this prospective, randomized, and double-blinded study. Following informed consent, subjects will receive 75 μg palonosetron or 4 mg ondansetron intravenously 20 to 30 minutes prior to anesthesia emergence. A standardized anesthetic and prophylactic dose of dexamethasone were administered to all subjects. Data was collected for 72-hours postoperatively and will include: verbal numeric rating scale for nausea, episodes of vomiting/retching, opioids administered, rescue antiemetics administered, and satisfaction with nausea control score (Likert scale). Results: 84 subjects were enrolled, 78, of which were used for analysis. Data analysis found significant differences between groups for: overall satisfaction with nausea control (palonosetron - 74.4%, ondansetron - 38.5% completely satisfied); mean number of antiemetic rescue doses in 72-hours (palonosetron -0.4, ondansetron -1.1); and incidence of nausea in patients with all four risk factors (palonosetron – 40%, ondansetron – 100%). Conclusions: There was no difference in the incidence and severity of postdischarge nausea and vomiting between high risk female patients receiving the prophylactic combination of palonosetron and dexamethasone vs. ondansetron and dexamethasone

Acute Mountain Sickness at Moderate Elevations

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations. Mitigation and treatment of neurotrauma.

Abstract

Few studies have evaluated high altitude headache (HAH) and acute mountain sickness (AMS) in military populations training at moderate altitudes (2000–3000 m). In the current study, researchers interviewed active-duty personnel training at Marine Corps Mountain Warfare Training Center. Participants were asked about HAH and AMS, risk factors, and treatments used. In a sample of 192 Sailors and Marines, 14.6% reported AMS (Lake Louise Criteria ≥3) and 28.5% reported HAH. Dehydration and recent arrival at altitude were significant AMS risk factors; dehydration and decreased sleep allowance were significant HAH risk factors. Among AMS-positive participants, ibuprofen users had increased likelihood of reporting threshold AMS than non-ibuprofen users (Fisher's exact test, one-sided, p < 0.05). These results suggest that maintenance of hydration and adequate sleep allowance are critical performance requirements at altitude. Further, ibuprofen may be a reasonable treatment for the symptoms of AMS and HAH. Further study is warranted to determine if ibuprofen may be a useful prophylaxis for these conditions

Monitoring Cortical Hypoxia using Near-infrared Spectroscopy: **Research and Application for Aviation Mishap Prevention**

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Research Priorities and Gaps: Casualty prevention.

Abstract

Introduction: Hypoxia remains one of the most significant physiologic hazards faced by military pilots and aircrew. For example, from May 2001 to March 2009 the Navy reported 64 hypoxia-related events in the F/A-18 community alone. These included three class-A mishaps, costing three lives and over \$200 million in lost aircraft. In the event of an oxygen delivery failure, poor mask fit, or hose leak, mishap prevention may depend solely on a pilot's recognition of hypoxia symptoms before cognitive function is significantly impaired. To mitigate this risk, the identification of valid and reliable in-cockpit hypoxia monitoring technologies is critical. Objective: The present study investigated the utility of near-infrared spectroscopy (NIRS) to monitor O2 saturation in the cerebral cortex as a first step toward a real-time, incockpit hypoxia monitoring capability. Methods: Twenty participants were exposed to air mixtures equivalent to 18,000 feet ASL for thirty minutes using the Reduced Oxygen Breathing Device (ROBD). During exposure and recovery, participants completed a series of reaction time tasks and were fitted with two NIRS sensors on the forehead. A pulse oximeter was placed on the index finger of participants' nondominant hand. Results: Analyses showed that NIRS measurements of the cerebral cortex responded to changes in blood O₂ concentration faster than finger pulse oximetry. Additionally, a strong positive correlation was found between cognitive performance and NIRS measurements throughout hypoxic exposure and recovery. **Discussion:** Results indicate that NIRS measurements of O₂ concentrations in the cerebral cortex may provide a more accurate and timely indication of an individual's functional state than pulse oximetry. While NIRS technology shows promise for cognitive evaluation, more research is needed to determine the reliability, validity, and suitability of the forehead-mounted sensor under ecologically valid cockpit conditions. Effective hypoxia mitigation would directly support ONR research initiatives for casualty prevention.

A Chaotic Analysis Method for Examining Speech

Authors and Affiliations

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Research Priorities and Gaps: Casualty prevention.

Abstract

Deterioration in speech is used as an indicator of an individual's decline in functioning. However, the development of an automated technology to detect this impairment is still in process. The underlying rationale for developing this type of technology is clear. Speech, a direct function of the brain, should be a channel for reflecting brain damage or disruption of function and, because speech is ubiquitous, it would represent a widely available and non-intrusive marker. Shiomi's Cerebral Exponent Calculation Algorithm (SiCECA) is a chaotic analysis method of evaluating human speech for signs of operator impairment. The SiCECA automated technology primarily utilizes vowel sounds and quantifies the amount of fluctuation in uttered speech. The rationale is that when a speaker is well rested and has no neurocognitive impairment the "strange attractor," a multi-dimensional mathematical figure derived from patterns in speech, contains a chaotic final set of properties and is depicted in a chaotic manner. In recent work, speech was recorded in a sleep deprivation/sleep restriction protocol and analyzed using SiCECA. Twenty individuals participated in both portions of the protocol. Preliminary results from the sleep deprivation paradigm showed a deflection in the SiCECA metric that corresponds to sleep-deprived time points and also corresponds to an increase in response lapses on the Psychomotor Vigilance Test (PVT). An echo of this relation was seen in the sleep restriction paradigm but to a lesser degree. These results show indication that this technology is capable of detecting fatigue. The validation of this technology is ongoing, with current studies looking at real time processing rather than processing of recorded speech. Application of such technology as a real time, non-intrusive indicator of operator state would represent an important advance in transportation safety.

Use of Microarray to Examine Neurotoxic Potential of Middle Eastern Sand: Relevance to Exposed U.S. Military Troops

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Research Priorities and Gaps: Mitigation and treatment of neurotrauma. Other conditions directly relevant to injuries on the battlefield.

Abstract

Introduction: Military personnel deployed to the Middle East have concerns regarding exposure to elevated levels of dust generated from blowing desert sand. Results from the Millennium Cohort Study substantiate these respiratory health concerns. Metals and harmful chemical components present in Middle Eastern sand have been identified as contributing factors for toxicity. Recent work in our lab has shown that soluble components of Afghanistan sand can be toxic and leads to apoptosis in a neuronal cell culture model. However, the exact mechanism of sand toxicity has not yet been identified. **Objective:** To evaluate particulate matter (PM)-induced neurotoxicity using microarray technology and to investigate whether sand-dust induced neurotoxicity could up-regulate the expression of apoptotic genes related to cell death pathways in correlation with cytotoxicity. Methods: Neuronal cells (MES 23.5) were exposed to different concentrations of soluble sand extracts and Microarray analysis of gene expression was carried out using the Affymetrix GeneChip System. Results: Gene Ontology analysis identified over 200 candidate genes which were significantly related to cell cycle and apoptosis, in particular Endoplasmic Reticulum stress related, mitogen-activated protein kinase and the p53 pathway, which may be involved in this cellular apoptotic response to sand exposure. Conclusion: Results of this study provides novel insight that relatively short-term exposure to PM can up-regulate apoptotic pathways in cells, potentially increasing the risk for neurodegeneration. Understanding differentiation in gene regulation is essential for the development of therapeutic approaches in neurodegenerative processes. These data provide a useful basis for screening candidate targets for early diagnosis and further intervention in PM-induced toxicity of neural cells. Future animal studies are warranted and may lead to a strategy for mitigating sand-dust induced neurotoxicity in our troops, which is a research need identified by the Office of Naval Research.

Deployment of a Fellowship-Trained Emergency Ultrasonographer with a Marine **Expeditionary Unit: Case Series of Point-of-Care Ultrasound Use**

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Research Priorities and Gaps: Medical systems support for maritime and expeditionary operations. Advanced forward care.

Abstract

Background: The 15th Marine Expeditionary Unit (MEU) deployed in support of WESTPAC 10-1 with a Shock Trauma Platoon containing a Fellowship-Trained Emergency Ultrasonographer. This was the first MEU to deploy with this advanced point-of-care ultrasound imaging capability. **Objectives:** To describe the use of advanced point-of-care ultrasonography in the setting of a MEU. Methods: A case series of medical conditions requiring the use of point-of-care ultrasonography during a 7-month MEU deployment will be presented. The positive and negative aspects of this advanced imaging capability in the setting of a MEU will be discussed. Results: A total of 32 point-of-care ultrasound studies were performed during the MEU. The ultrasound studies performed (number of studies done) included appendiceal (2), biliary (1), echocardiography (2), inguinal (2), musculoskeletal/soft tissue (5), ocular (2), pelvic (9), renal/bladder (3), scrotal (4), and deep venous thrombosis (2). Ultrasound-guided procedures performed included fracture reduction (1) and incision & drainage (2). Diagnoses confirmed with ultrasound include abscess (2), cellulitis (2), distal radius fracture (1), retinal detachment (1), live intrauterine pregnancy (4), completed abortion (1), epididymitis (1), and varicocoele (1). Serious conditions that were excluded with ultrasound included gallstones/cholecystitis, pericardial effusion, inguinal hernia, ectopic pregnancy, urolithiasis, testicular torsion, testicular mass, and deep venous thrombosis. Conclusions: Advanced point-of-care ultrasonography is a useful tool to both rule-in serious conditions and expedite their care as well as exclude them and avoid potential MEDEVAC scenarios during a MEU.

Past Use, Present Proficiency, and Future Utility of Point-of-Care Ultrasound in the Operational Environment - A Survey of US Navy Healthcare Providers

Authors and Affiliations

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Research Priorities and Gaps: Other conditions directly relevant to injuries on the battlefield. Medical systems support for maritime and expeditionary operations. Advanced forward care.

Abstract

Objectives: To assess how US Navy healthcare providers have utilized point-of-care ultrasound (POCUS) while deployed, their current proficiency in POCUS, and future POCUS training needs prior to deployments. Methods: Research data derived from an approved Naval Medical Center, Portsmouth, VA IRB/IACUC protocol. US Navy healthcare providers who had deployed while providing direct patient care were voluntarily surveyed utilizing a validated on-line survey. The providers surveyed included physicians, nurses, physician assistants, and hospital corpsmen. Comparative and descriptive statistics were applied to the survey results. Results: 293 of the 331 (88.5%) providers that met the inclusion criteria completed the survey. 219 (66.4%) of the providers were physicians and 111 (33.6%) were nonphysicians. 185 of 330 (56.1%) providers had a POCUS machine available and 142 (76.8%) of them used it. The three most common POCUS applications used while deployed were the focused assessment with sonography for trauma or FAST exam (84 of 142 providers, 59.1%), pelvic US (62/142, 43.7%), and gallbladder US (41/142, 28.9%). 149 of 328 (45.4%) reported current proficiency in POCUS. The three POCUS applications with the highest self-reported proficiency on a 5-point scale were pelvic US (3.96 mean rating), FAST (3.78), and bladder US (3.37). The three POCUS applications with the highest estimated future utility in the operational environment as rated on a 5-point scale were the FAST exam (4.25), pelvic US (3.84), and testicular US (3.54). The POCUS applications with the greatest difference in future utility and current proficiency were appendiceal US (1.65 mean difference) and testicular US (1.61). Conclusions: The majority of deployed US Navy healthcare providers who had a POCUS machine available used it. The most common POCUS applications used were the FAST exam, pelvic, and gallbladder. The POCUS applications with the largest future utility were pelvic, the FAST exam, and testicular. The greatest deficits in current proficiency versus future utility are in appendiceal and testicular ultrasound.

Changes in Blood Levels of S100B and Corticosterone after Mild Traumatic Brain Injury (TBI) and Hemorrhagic Shock (HS) in Wistar Rats

Authors and Affiliations

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Research Priorities and Gaps: Traumatic brain injury and PTSD. Mitigation and treatment of neurotrauma

Abstract

The present conflict in Iraq and Afghanistan has led to an increase in TBI, resulting from IEDs. Reliable diagnostics are needed to better diagnose and treat TBI. The goal of this study was to evaluate plasma for biomarkers of neurotrauma and general physical stress in rats with mild TBI accompanied by severe hemorrhage. The biomarkers studied were S100B and corticosterone. S100B, a calcium binding protein found mostly in astrocytes in the brain, is linked to the severity and outcome of TBI. Corticosterone, a stress hormone in rats (equivalent to cortisol in humans), may also be used as a biomarker of stress.

At various time intervals up to 2 h, plasma samples were collected from rats subjected to closed-head, acceleration impact TBI, with or without severe (40% EBV) hemorrhage. An enzyme immunoassay specific for S100B, using commercially available antibodies, was used to test the rat plasma samples. The standard curve using 19 pg/ml - 10 ng/ml purified bovine S100B, yielded a linear regression line (R² = 0.99). Samples were also tested for corticosterone using a commercially available enzyme immunoassay kit.

S100B was detected in samples from rats with TBI and severe controlled hemorrhage, but not significantly in non-injured control rats. Preliminary results suggest a correlation between the levels of S100B and the severity of injury. Corticosterone levels also correlated with the level of injury. Larger test groups will be generated to determine if the differences in S100B and corticosterone are significant. These assays may provide a means to rapidly diagnose TBI.

This work was supported by Office of Naval Research funded work unit number 602236N.4420. 1094. A0601 and USAMRMC Contract No. W81XWH-09-2-0123.

Prospective, Randomized, Double-Blind, Placebo-Controlled Investigation Evaluating the Effects of Perioperative Administration of Gabapentin in Patients Undergoing Shoulder Arthroscopy with a Combination of General Anesthesia and Interscalene Nerve Block

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Research Priorities and Gaps: Warfighter restoration.

Abstract

Introduction: Shoulder arthroscopy is one of the most common orthopedic procedures performed on active duty personnel. Unfortunately, postoperative pain can be severe and delay recovery of the warfighter. Recent studies suggest gabapentin has opioid-sparing effects and may reduce acute postoperative pain. However, there is limited research on the efficacy of gabapentin when combined in a multimodal approach after shoulder arthroscopy under general anesthesia with an interscalene block. **Methods:** A prospective, double-blind study of 70 subjects randomized to receive either 300 mg gabapentin or placebo one hour prior surgery, then twice a day for two days. The primary outcome was average pain scores. Secondary outcomes included differences in morphine equivalents, side effects, and sleep patterns, Results: No significant differences in pain scores were found on day #1 (gabapentin: 4.23) \pm 2.61 vs. placebo: 4.61 \pm 2.57, P = .58) or day #2 (gabapentin: 4.26 \pm 2.39 vs. placebo: 4.03 \pm 2.34, P = .71). Total morphine equivalents on day #1 (gabapentin: 9.75 ± 6.58 mg vs. placebo: 9.52 ± 4.75 mg, P = .88) and day #2 (gabapentin: 9.21 ± 6.66 vs. placebo: 6.93 ± 5.44 , P = .17) were similar. Side effects and sleep patterns were similar (P > .05). Conclusions: These results suggest this dosing regimen of gabapentin is not efficacious in improving outcomes in patients undergoing shoulder arthroscopy under general anesthesia with an interscalene block. Future studies are needed on the effect of single and multiday gabapentin regimens on postoperative pain, and should incorporate measures of side effect severity and include objective measures of adherence.

A Descriptive Pilot Investigation Evaluating Physiological and Psychological Stress Measurements in Patients Presenting for Elective Surgical Procedures

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Abstract

Introduction: Anticipation of surgery is a significant stressor that can lead to abnormal or excessive activation of the stress response. The purpose of this study was to evaluate preoperative stress measurements in patients presenting for elective outpatient general surgery procedures. Methods: This prospective, descriptive, correlational pilot study evaluated 29 ASA I & II patients for elective general, non-cancer surgical procedures. Measures of state affect (Multiple Affect Adjective Checklist (MAACL-R), subjective stress (Visual Analogue Scales for stress (VAS-S)) and thermal comfort (VAS-T) were collected on admission (Time 1), at arrival in preoperative area (Time 2), and prior to entering the OR (Time 3). Salivary alpha amylase (SAA) samples were collected at each time point to evaluate the SNS stress response. **Results:** The majority of subjects were men (n = 17, 58.6%), with n = 12 (41.4%) having no past surgical history (PSH). SAA levels were significantly higher at Time 2 as compared to Time 1 $(220.36 \pm 183.8 \text{ U/ml} \text{ vs. } 160.53 \pm 120.92 \text{ U/ml}, P = .012)$. VAS-S were significantly higher at Time 2 (VAS-S: 36.6 ± 25.19) and Time 3 (VAS-S 38.82 ± 26.28) as compared to Time 1 (27.06 ± 21.6) (P<.05). There was a trend toward lower positive affect (PA) (MAACL-R) at Time 3 vs. Time 1 (mean difference: -2.27 ± 6.55 , P = .07). Lower PA was negatively correlated with SAA at Time 2 (r = -.384, P = .04). Subjects who reported feeling colder (VAS-T) in the preoperative area had significantly higher increase in SAA levels (r = -.556, P = .003). This relationship was stronger in subjects with no PSH (r = -.869, P < .001). Conclusion: Pilot study results suggest the preoperative period is associated with increased physiological and psychological stress. Further studies are needed to determine if any of these stress measurements are predictors of perioperative outcomes.

The views expressed in this abstract are those of the authors and do not reflect official policy or position of the Department of the Navy, Department of Defense, Uniformed Services University of the Health Sciences, or the United States Government.

Lyophilized Platelet Transfusion Does Not Constitute an Immunologic "Second Hit" in a Non-Human Primate Hemorrhagic Shock Model

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Research Priorities and Gaps: Other conditions directly relevant to injuries on the battlefield. Rapid blood treatment. Multifunctional blood substitute and multifunctional resuscitation fluids.

Abstract

Background: Apheresed platelet concentrates accumulate biologic response modulators (BRMs) with prolonged storage. Platelet processing by lyophilization offers the potential for long term platelet storage and transfusibility. Lyophilized platelets (LP) are preserved in a metabolically inactive state until rehydrated in sterile water. We hypothesized that LP transfusion will not constitute an immunologic "second hit." Methods: Rhesus Macaques were anesthetized and subjected to grade III hemorrhagic shock to induce a systemic inflammatory profile consistent with an immunological "first hit." To determine the "second hit" capability of LP, 2×10^{10} reconstituted LP were infused at 15 minutes following the initiation of shock. In parallel experiments, normal saline (NS) or 2×10^{10} fresh (day 1 – 3) apheresed human platelets were infused at 15 minutes following initiation of shock to serve as controls. Subsequently, volume resuscitation with additional normal saline, per ATLS guidelines, was performed and all animals survived for 480 minutes post-shock initiation. Physiologic parameters were continually monitored; serum collected immediately preceding shock and supernatants from the LP and FAP were assayed for pro-inflammatory cytokines. All cytokine detection was performed on a Luminex IS 100. Results: Grade III hemorrhagic shock, determined by a reduction in MAP and blood loss index, resulted in a significant pro-inflammatory response determined by significant changes in the serum levels of IL-6 and IL-8 in NS controls. The FAP supernatant contained increased concentrations of TNFα, MCP1, IP-10 and IL-8 as compared to LP. Conclusions: The model utilized in this study effectively constitutes an immunological first hit as determined by altered systemic levels of IL6 and IL8 in response to the hemorrhagic shock. The inflammatory profile of LP treated animals was not different than NS control or FAP treated animals, indicating that lyophilized platelet transfusion does not constitute an immunologic second hit in the setting of hemorrhagic shock.

The Early Post-Hemorrhage Coagulation Profile is Characterized by Qualitative Platelet Dysfunction

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Research Priorities and Gaps: Wound / injury management throughout the continuum of care. Rapid blood treatment. Multifunctional blood substitute and multifunctional resuscitation fluids.

Abstract

Background: Development of a Rhesus Macaque model of hemorrhagic shock, an isolated qualitative platelet dysfunction from baseline, was suggested; this observation is supported by clinical reports dating to the Vietnam era. Our group hypothesized that qualitative platelet dysfunction is an early component of the post-hemorrhage coagulation profile. **Methods:** Rhesus Macaques were anesthetized and a 60% transverse left hepatectomy performed with no attempt at hemorrhage control to induce grade III hemorrhagic shock. Fifteen minutes after injury, 50ml of normal saline (NS) or 2×10^{10} fresh apheresed human platelets (FAP) were administered. Subsequent volume resuscitation utilized NS per ATLS guidelines. At T=120 laparotomy was performed, operative hemostasis achieved and blood loss was measured. Physiologic parameters were continually monitored and ROTEM EXTEM and FIBTEM, CBC and ABG analysis performed throughout procedure. Results: Grade III hemorrhagic shock was induced as indicated by a reduction in MAP from T=0 with a blood loss index of 27.5% in NS controls. ROTEM EXTEM analysis: significant increase in clot formation time (CFT) and reduction in α angle at T=60-480 from baseline in NS controls; FAP treated animals had no significant change in CFT or α angle T=0-480. ROTEM FIBTEM analysis: No significant change in CFT or α angle in NS or FAP treated animals. Platelet count decreased significantly at in NS controls and at in FAP treated. The controls also showed a significant decrease in hematocrit from. Discussion: Results demonstrate platelet dysfunction early following hemorrhagic shock as evidenced by isolated changes in ROTEM EXTEM α and CFT parameters from baseline in NS controls; these changes are avoided by FAP administration. Furthermore, changes in platelet function occur prior to significant changes in platelet count and in the absence of clinical thrombocytopenia. In this Rhesus Macaque model, the early post-hemorrhage coagulation profile is characterized by a qualitative platelet dysfunction.

Computational Analysis and Optimization of the Rhombic Flap Wound Closure

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Research Priorities and Gaps: Wound management.

Abstract

Objectives: 1) Develop a hyperelastic computational model of skin viscoelastic properties for analysis of wound closures, and 2) Apply the model to variations of the rhombic skin flap to quantify closure force vectors and optimize wound closure tension. Methods: A computational model utilizing the finite element method was created to simulate skin defect closure employing rhombic transposition flaps. Variables of transposition angle, flap width, and tissue undermining were analyzed. Outcome measures of tissue stress, strain and wound distortion were evaluated and optimized for a standard defect. Results: 2nd order Yeoh hyperelastic model was fit to previously published experimental skin data with good approximation of observed properties. In the analysis of transposition flap closures of the 60-120 degree rhomboid defect, the model suggests that a biomechanically ideal flap design is constructed with distal flap angle of 30 degrees, as is employed in the Webster flap, with the donor site near margin oriented parallel to the short axis of the defect, as in the traditional Limberg flap. This configuration minimizes peak tissue stress and strain and most evenly distributes wound tension across the closure line. **Conclusions:** The model quantitatively demonstrates several recognized principles of the rhombic flap. Square defects, as compared to rhomboid defects, close with lower tissue strain, but form a larger standing cutaneous deformity. The Webster flap best distributes wound tension across the incision line and the Dufourmental modification alters the closure force vector. These principles may be considered in wound closure planning to minimize scarring and wound dehiscence. The findings of this study are directly applicable to wound management practices impacting Department of Defense personnel and can help surgeons minimize the disfiguring sequelae of soft tissue injury.

Assessment of Environmental Tobacco Smoke Exposure in U.S. Navy Submariners

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Research Priorities and Gaps: Undersea medicine—diving and submarines.

Abstract

The effectiveness of the U.S. Navy and Marine Corps Tobacco Policy in protecting submariners from Environmental Tobacco Smoke (ETS) was evaluated. Exposure to ETS was measured using urinary cotinine as a biomarker. Subjects were recruited from 9 U.S. Navy submarines. Non-tobacco users were identified and provided two urine samples (1. pre-deployment, in harbor; 2. deployed, at sea) to quantify exposure to ETS and the magnitude of any change. Samples were analyzed using liquid chromatography tandem mass spectrometry (LC-MS/MS). Overall, deployed cotinine levels were 2.1 times as much as in port levels in non-tobacco using submariners (95% CI: 1.8 to 2.4, p <0.001). This study provides evidence that non-tobacco using submariners were being exposed to ETS. Exposure was seen in all submarine classes and was not limited to personnel working in proximity to the smoking area.

This study prompted an immediate review of the U.S. Navy and Marine Corps Tobacco Policy in protecting submariners from ETS, and On 8 April 2010 Commander, Submarine Forces (COMSUBFOR) established a policy banning smoking below decks aboard all U.S. Navy submarines effective 31 December 2010. The study and policy change also lead to a COMSUBLANT/COMSUBPAC notice on 2 August 2010 outlining the Submarine Force Tobacco Cessation Program and encouraging commands to accelerate the program's implementation.

This project was funded through the NAVSEASYSCOM 05/087.

Human Injury and Treatment

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Research Priorities and Gaps: Human injury and treatment model—(1) crew medical assessment and (2) crew complement response.

Abstract

Over the last several years, the US Navy has invested in the development of computer models that simulate the effects of explosions on ships and shipboard equipment. Little effort has been expended, however, on models to reliably simulate the effects of explosions on the crew. Unfortunately, casualty modelling is required to satisfy federally mandated Testing and Evaluation requirements and is essential to verifying adequate personnel and cross-training of personnel and determining medical response requirements. To address this need, the Office of Naval Research is developing a computer modelling tool for predicting human injury, incapacitation, and medical response requirements associated with blast attacks in shipboard environments. Specifically, this modelling tool will be able to measure, track, and determine the extent of human injury, treatment options, and ability to return personnel to duty, and document onboard personnel outcome assessments (including fatality reporting) with great accuracy. It will assess the most taxing injury and treatment conditions, such as weapon hits, and provide probabilistic roll-up results for a large number of realistic hit points and resulting injury scenarios. This modelling capability will take into account shipboard medical allowance designation (supplies), available medical personnel, personnel training levels, the ship's operating condition (normal sailing or battle engagement), injury progression (degradation of injuries prior to treatment), and confounders (other conditions that would modify the treatment given). This presentation unveils the results of the first year of development of the Human Injury and Treatment (HIT) model, and provides an overview of the technical approach and Science and Technology advancements scheduled over the next four years.



- New-onset lupus and RA

 Self-report of either outcome at follow-up (2007-2008) among participants with no prior condition
 Study population: lupus (N = 19,157) and RA (N = 18,848)

Respiratory symptoms and conditions Respiratory symptoms (study population: N = 22,297)

osure was umed if loyment was to a tion within a 2-, r 5-mile radius i the burn pit	Exposure was measured by summing the days deployed near the burn pits between 2003 and the 2007-2008 questionnaire	Participants deployed to multipl camp sites were categorized based the camp to which they were deployed			
	Categorized into	with the longest			

isks in the Millennium Cohort Study

PH^e; Nisara S. Granado, MPH, PhD^e; Isabel G. Jacobson, MPH^e; Edward J. Boyko, MD, MPH^e; Christopher J. Phillips, MD, MPH^e; and Tyler C. Smith, MS, PhD^e for the Millennium Cohort Study Team

: Research and Information Center, Department of Veterans Affairs Puget Sound Health Care System, Seattle, Washington; alft Sciences, Bethesda, Maryland; "Analytic Services, Inc. (ANSER), Arlington, Virginia; and al Camp Pendleton, Camp Pendleton, California.



		Deployment						
		Other	1.00					
0.96 - 1.16		Exposed	2.11	0.91 - 4.92		1.17	0.83 - 1.64	
		Exposed days			0.17			
0.82 - 1.14			1.91	0.40 - 9.05				
			2.00			1.47		
			3.37	0.97 - 11.71				
		>211						
	0.36	Camp site						0.34
		No exposure	1.00					
0.96 - 1.22		Balad						
		Taji				1.24	0.64 - 2.41	
0.81 - 1.14						0.74	0.34 - 1.63	

	0.94 - 1.13			0.67 - 1.24						
		0.94								
			1.00							
	0.83 - 1.17		1.00			0.71				
	0.88 - 1.25						0.41 - 1.45			
	0.88 - 1.26		1.10	0.64 - 1.90			0.68 - 1.96			
	0.87 - 1.23		0.90			1.14	0.41 - 1.45			
Э										
	0.90 - 1.14		1.07	0.74 - 1.54		0.84	0.56 - 1.24			
	0.90 - 1.36		1.05							
	0.85 - 1.21									

95% confidence interval (CI) are adjusted for demographics, military characteristics, smoking status, and other

...

ignificant findings for lupus, RA, or any of the ptoms and conditions

of a burn pit after adjusting for separation status Cl:1.01–1.21)

wait

re was not signinicantly associated with increased the outcomes when compared with Camp Arifjan erification (for lupus and RA only) lupus cases and 10/98 RA cases among active-dut

vere diagnosed while in the service re was not significantly associated with the smoke plume during burning operations,

- Inability to account for many other in-theater exposures
 Inability to account for many other in-theater exposures
 such as exposure from particulate matter, fuel, or those related to specific occupations; however had the ability
- This is the first study to investigate whether proximity to a burn pit is associated with CMI, new-onset lupus and
- Large sample size that is representative of US military personnel; enhanced statistical power for assessing expected the same associations.

Conclusions

- These results suggest no overall consistent elevated risk of self-reported CMI, lupus, RA, or respiratory symptoms and conditions for those who deployed within a close proximity of a documented open-air burn pit
- This study should be considered an important first look into health concerns potentially associated with smoke exposure from open-air burn pit
- More robust person-level exposure data are needed to understand the complex continuum of deployment related exposures and how these may impact short- and long-term health conditions

Acknowledgements

The Millensium Cahert Shary (see reclaids Melissa Bayrell, Gins Creave, Nacy Corn Cardino, James Darles, Jose Guntals, Nation Canada, Camer Hermand, James Horis, Label Acc bert, Poly Jones, Lazeri Kipp, Cyritha Lazeri Minn, Terir Laler, Gorden Lysch, James McGree, Hope Fordy, Jones Shary, Sander Steel, Poly Jones McGree, Hope Jones Shary, Frenchy Vodel, Mellen Welder, Barbary, Frenchy Vodel, Mellen Welder, Debegree, French Vodel, Mellen Welder, Debegree, French Welder, Mellen Welder, Land Hermand, French Welder, Debegree, Cardina, French Welder, Mellen Welder, Mellen Welder, Gereger, Ger

Additionary for addition into Social Segretain Area Americans, Service Services, Americans, from the Management Information Dission, USD Entered Management Learning (Services), Americans and America

Traview expressed in this research are those of the authors and do not necessarily reflect the discussoring opening on the Department of the New Department of the Arm. Department of the Arm. Department of the Arm. Department of Defense, Department of Test and Veterans Affairs, or the US Government. Human subjects a participated in the study after giving time free and informed convent. This invessed has been consisted in come/lance with all applicable Federal Regulations governing the Protection of Human Obstants in Demand.

We are indebted to the Millennium Cohort Study

Photo courtesy of defenseimagery.mil







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